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AUTHORITY

USAMRMC ltr, 19 Jan 2001.

AD_____

Award Number: DAMD17-97-2-7003

TITLE: Effects of Diet High in Palmitoleic Acid on Serum Lipid
       Levels and Metabolism, Phase 2

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REPORT DATE: July 2000

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
               Fort Detrick, Maryland 21702-5012

DTIC QUALITY INSPECTED 4   20000627 157

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE July 2000	3. REPORT TYPE AND DATES COVERED Final (15 Mar 97 – 14 Jun 00)

4. TITLE AND SUBTITLE
Effects of Diet High in Palmitoleic Acid on Serum Lipid Levels and Metabolism, Phase 2

5. FUNDING NUMBERS
DAMD17-97-2-7003

6. AUTHOR(S)
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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

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12b. DISTRIBUTION CODE

13. ABSTRACT (Maximum 200 Words)

A randomized crossover feeding study with a macadamia nut and oil based high monounsaturated fat diet(HIMUFA) and a typical American diet high in saturated fat(HISAT) was conducted on 27 healthy men and women aged 20 to 52. Fatty acid profiles were HIMUFA: 22%MUFA,9%SFA;HISAT:11%MUFA,20%SFA. Each diet was consumed for 8 weeks with a 2-month wash-out. Fasting plasma lipids and lipoprotein subclasses by using NMR or chemical analysis were measured on week 5 and the last two consecutive days of week 8 in each diet period. Isoenergenic substitution with 11% Kcal MUFA for SFA significantly reduced plasma total cholesterol, LDL, HDL, VLDL and TG(in NMR). A small but significant reduction in both LDL and HDL particle size in the HIMUFA diet compared to the HISAT diet. These were due to the reductions in larger particles- L3, and HDL2(H5,H4). LDL particle concentrations in parallel with LDL levels were significantly reduced in the HIMUFA diet. The cholesterol lowering effects in total cholesterol and LDL of the HIMUFA diet are very prominent. Macadamia nut based MUFA can be a good alternative for SFA in the diet to lower CHD risks. Further investigations are warranted to evaluate the long-term beneficial effects of HIMUFA on CVD risk.

14. SUBJECT TERMS
Serum Lipids, Congressional Interest

15. NUMBER OF PAGES
70

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited

FOREWORD

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INTRODUCTION

Monounsaturated fatty acids have the potential of providing high energy density foods without the increased cardiovascular disease risk that is associated with high fat diets or with very low fat diets. The aim of the study was to evaluate the effects of a macadamia nut based diet high in monounsaturated fatty acids on plasma lipids as compared to a typical American diet high in saturated fats. Of special interest, was to speculate plasma lipoproteins and their subclasses in response to dietary fats. A complete set of lipoprotein profiles were measured by Proton Nuclear Magnetic Resonance Spectroscopy (NMR), which included the subclasses of HDL, LDL, VLDL and particle concentrations of LDL as well as the mean particle size of each lipoprotein. Macadamia nuts and oil provided the primary fat sources high in palmitoleic acid for the high monounsaturated fat diet. There is also potential in the development of healthy energy dense dietary products that are originated from natural food resource (i.e. macadamia nuts) for use by the men and women of our armed forces in the forms of Meals Ready to Eat. Twenty-seven healthy free-living participants completed two feeding periods. They were 13 men and 14 women, aged between 18 to 52 years old. Of the total 27 participants, approximately 30 percent were Caucasian, 56 percent were Asian-Pacific islander, and 15 percent were mixed with Asian and Caucasian. They had normal blood pressure to mild hypertension. The baseline cholesterol ranged from desirable to borderline high based upon the NCEP guidelines.

BODY

I.   Methodogy

I-1 Study Design

This investigation was a controlled, randomized, two by two crossover feeding study design comparing two diets, one diet high in MUFAs (HIMUFA) and one diet high in SFAs (HISAT) over two periods. Each diet period lasted 54 days (approximately 8-weeks). An initial run-in period of 5 days, in which both study diets were eaten, was used to screen subjects for compliance and willingness to accept the restrictions imposed by the dietary regimens. After completion of the run-in period the study subjects were randomly assigned to one of the study diets for the first study period which was blocked by gender. At the end of the 1st period there was a two- month wash out in which participants returned to their normal diet patterns. After this two-month period the subjects returned to the study and were then switched to the other diet for the second study period.

I-2 Recruitment

Informed Consent

The study was reviewed and approved by the Human Research Committee of the University of Hawaii. After a brief screening for exclusion criteria, informed consent was obtained from each subject prior to any blood tests being done or any diet given. Informed consent by proxy was not accepted.

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Inclusion/exclusion Criteria

All potential subjects were initially screened for health exclusion criteria. Persons with plasma cholesterol level below 180mg/dl were excluded since such a subject might be less responsive to dietary intervention. All subjects were required to be between 18 to 55 years of age, and had plasma total cholesterol levels of between 180 and 240mg/dl. A history of allergy to tree grown nuts, diabetes mellitus or pancreatic insufficiency, hypertriglyceridemia (fasting triglycerols level over 400mg/dl), current pharmacologic treatment for hyperlipidemia, or an unstable medical condition were excluded. Subjects receiving medications for chronic medical conditions such as hypothyroidism, or certain types of oral contraceptives, or who had stable and controlled mild to moderate hypertension were allowed to enter the study on the condition that the medication that they took was long-term and was unlikely to change in dosage or character during the study. Pregnancy and breast-feeding were exclusion criteria for this study.

Recruiting

Recruitment of subjects began August 25, 1997 and continued through September 22, 1997. Posters and flyers were placed on bulletin boards throughout the University of Hawaii at Manoa. Advertisements were also placed in the University's student newspaper. Volunteers were directed to contact investigators by telephone or email if they were interested in receiving more information about the study. Approximately four hundred and ten inquiries were received during the recruitment period. Of these four hundred and ten inquiries, two hundred and

forty–eight volunteers completed a screening interview over the telephone. One hundred and fifty-two out of these two hundred and forty-eight people received screening blood tests to determine cholesterol levels. Fifty-five persons who had a blood screen test were eligible as potential participants based upon their cholesterol levels. The baseline evaluation consisted of a medical, dietary, and family history and a blood laboratory test. Blood tests included fasting blood sugar, total cholesterol, TG, kidney and liver function. These tests were conducted by Diagnostic Laboratory Services.

Study participants

Thirty-five participants (18 men, 17 women) were selected to enter the 5-day run-in period of the study. Participant interviews were performed in order to screen and evaluate compliance of the potential participants. Ultimately one male was excluded due to concerns regarding compliance with the study protocols. Therefore, thirty-four (17men, 17 women) entered the study feeding. The participants were randomly assigned to either the HIMUFA diet or the HISAT diet, which was blocked by gender. In week four, one male dropped from the study due to back injury and difficulties in traveling daily to the study site. Thirty-three participants continued until the end of the first feeding period. After a two-month washout period, six participants (3 women, 3 men) dropped out the study. Twenty-seven participants completed the second period of the feeding study.

I-3 Dietary intervention

Participant compliance

During each study period, each subject had to eat only the food that was provided except for a free meal on Saturday night. The subjects had to eat their morning and evening meals at the feeding center while under surveillance of study staff during weekdays. Packed lunches were provided to the subjects. On weekends the subjects ate a brunch at the feeding center under surveillance of study staff, a packed Sunday dinner in a micro-wavable container was given to participants to be heated and eaten at home. All participants were required to eat all the foods that were provided to them.

As stated earlier, the Saturday meal was designated as a "free" meal allowing the subjects to eat away from the feeding center if they so desired. This "free" meal was to follow dietary guidelines established by the study and was to be reported, in detail, to the nutritionist. An option to the participants was to have the Saturday meal provided by the center. Approximately half of the subjects chose to eat all meals from the study kitchen throughout the study.

Nutritional profiles

The two experimental diets were:

1) A high monounsaturated fat diet (HIMUFA) with 38% of calories from fat with a fat profile of 9% SFA, 7% PUFA, and 22% MUFA.

2) A "typical American" or high saturated fat diet (HISAT) with 38% of calories from fat with a fat profile of 20% SFA, 7% PUFA, and 11%

MUFA.

The percentage of calories derived from protein and carbohydrate was 15% and 47% respectively for both test diets. Cholesterol levels were held constant for both diets (300mg/day). A 12-day menu cycle was designed for the study, using the Food Processor (ver 6.0 Plus, 1994) and Nutrition Database System (NDS ver2.91, 1997). The menu cycle consisted of eight weekday and four weekend menus. All the meals were prepared with common food ingredients. Macadamia nuts and oil provided the major fat sources for the high MUFA diet. The percentage contribution of whole Macadamia nuts and oil to the MUFA content in the development of the menu was approximately 50% for each. The major fat sources for the high SFA diet was butter and coconut oil. Additionally four unit foods were provided as snacks. These were in the form of 100 kcal cookies, 150 kcal muffins and 200 kcal scones and muffins. These unit foods were developed to match the fatty acid and macronutrient profiles of the daily menu. Subjects were allowed to eat as much of the unit foods as they desired as long as their established body weight determined at the beginning of the study was maintained.

All beverages were required to be non-caloric. A limited amount of non-caloric caffeinated beverages were allowed (up to 5 cups of coffee or equivalent beverage per day). Up to five alcoholic drinks per week were permitted. A daily diary was used to record any deviation from planned food and beverage consumption during the study.

Daily energy intake needed to maintain body weight was estimated for each

subject according to Harris-Benedict equations based upon the individual's weight, height, and age at baseline. Calorie levels were adjusted whenever necessary to maintain each subject's weight throughout the study period. There were four different calorie levels for each study's daily diet. These were designed for each individual participant and ranged from 1700 kcal to 3000 kcal.

Meals were prepared individually for each participant. All the ingredients were measured to the 0.1g using OHAUS scales (CT-1200-S, Max:1200*0.1g). Large batch ingredients were measured to the 0.5g using Weight-Tronis scale(M3276, Max:5000*1/2 g). The scales were validated daily using student weight kits included 500g, 100g, 50g, 20g, 10g, and 5g (OHAUS) and were calibrated before each feeding period.

I-3 Measurements

Clinic measurements

The body weight of each study participant was measured in the morning before breakfast twice a week during the run-in period and once a week during the study periods. Participants were clothed in light clothing and these weighing sessions were conducted at the feeding site. Waist and hip circumference were measured at the first day of each study period. Pregnancy tests for all women were done monthly.

Blood pressures were taken each time that weight was measured. One reading was taken in a sitting position after five minutes of rest with a standard

sphygmomanometer by the project coordinator, who was certified with the standardized protocols and methods from the Honolulu Heart Program and the Family Blood Pressure Program (FBPP).

Three fasting bloods (twelve-hour minimum fasting) were drawn from each participant during each eight-week period of the study diet. The schedule for drawing blood consisted of one specimen in the fifth week and two specimens (on consecutive days) in the eighth week. Purple top EDTA tubes for plasma specimens were stored in an ice bath prior to processing. Specimens were centrifuged at 4^0 C for 10 to 15 minutes at 3,000g and plasma were then aliquoted into 0.5-ml cryovials for storage. Average processing time for the specimens was less than one hour from the drawing of the specimen to completion of processing. Completed aliquots were stored in dry ice before being transferred into a - 70^0 C freezer for storage.

Lipids analysis

A. Proton Nuclear Magnetic Resonance analysis

Proton Nuclear Magnetic Resonance (NMR) analysis was used to measure plasma lipids and lipoprotein profiles. These analyzes were done by LipoMed Inc. at their laboratories in North Carolina. The basic concept of NMR distinction between lipoprotein subfractions is the diameter of the lipid shell. This is due to the fact that lipoprotein particles with different shapes broadcast distinguishable NMR signals. A typical plasma NMR spectrum at ~0.8 ppm will contain signals

from the methyl groups of the four types of lipid present in the particles: phospholipid, cholesterol, cholesterol ester, and TG. The methyl signals from the different lipids in each particle are inherently different from one another, so they combine to produce a composite "bulk lipid' signal. The amplitude of the sound signal is expected to be linearly dependent on the number of the bells. Thus, a quantitative relationship exists between bell number and sound amplitude. NMR can also derive the mass of the bell by the conversion of a factor relating sound amplitude to bell mass. Quantification is achieved using a three-step process. This process consists of measurement of the plasma NMR spectrum followed by computer de-convolution of the spectral data and then calculation of the subclass concentration or mass.

NMR spectroscopy can quantify sixteen subclasses of VLDL, LDL, and HDL in frozen plasma specimens. In addition to the concentrations of these sixteen subclasses, NMR can determine concentrations of total cholesterol, total triglycerides, LDL, HDL, as well as LDL particle concentration, and average VLDL, LDL, and HDL particle size. NMR lipoprotein profile contains the following information:

7 chylomicron/VLDL subclass concentrations (in units of mg/dl triglyceride).
4 IDL/LDL subclass concentrations (in units of mg/dl cholesterol)
5 HDL subclass concentrations (in units of mg/dl cholesterol)
Total cholesterol (mg/dl)
VLDL triglyceride (mg/dl)
LDL cholesterol (mg/dl; includes IDL cholesterol)
HDL cholesterol (mg/dl)
VLDL size (mass-weight average diameter in nm)

LDL Size (mass-weight average diameter in nm; values > 20.5nm identify Pattern A values <or = 20.5nm identify Pattern B)
HDL Size (mass-weight average diameter in nm)
LDL Particle concentration (in units of nmol/L; analogous to LDL apoB measurement)

The estimated diameter ranges of the subclasses were determined by traditional electron microscopy measurements for VLDL and LDL subclasses and by polyacrylamide gradient gel electrophoresis for HDL subclasses. The lipoprotein subclasses quantified by NMR and their diameter ranges are listed below.

Chylomicron/VLDL subclasses:
Chylos: >200 nm
V6: 150 ± 70 nm
V5: 70 ±10 nm
V4: 50 ±10 nm
V3: 38 ± 3 nm
V2: 33 ± 2 nm
V1: 29 ± 2 nm

IDL/LDL subclasses:
IDL: 25 ± 2 nm
L3: 22 ±0.7 nm
L2: 20.5 ±0.7
L1: 19 ± 0.7nm

HDL subclasses
H5 (HDL2b): 11.5 ± 1.5 nm
H4 (HDL2a): 9.4 ± 0.6 nm
H3 (HDL3a): 8.5 ±0.3 nm
H2 (HDL3b): 8.0 ± 0.2 nm
H1 (HDL3c): 7.5± 0.2 nm

B. Chemical analysis

Measurements of frozen plasma total cholesterol, TG, HDL and blood sugar were conducted in the Native Hawaiian Health Research (NHHR) laboratory, which was certified by the CDC-lipid standardization program. Total cholesterol, TG, and HDL were quantified with CDC-standardized enzyme assays using a Beckman Synchron CX4 analyzer. HDL fractions needed to be separated from plasma LDL and VLDL. This separation was done by chemical precipitation techniques using dextran sulfate of 50kDa before the analysis. LDL cholesterol was derived using Friedewald estimation. This estimation could be used since none of the blood samples TG levels were over 400 mg/dl:

LDL cholesterol = total cholesterol – HDL cholesterol- (TG÷5)

* TG÷5 is an estimation of VLDL cholesterol

Food analysis

Food sample collections for food analysis occurred at random intervals throughout the diet period until a complete 12-day menu cycle was obtained. Samples of each meal were randomly selected from the study kitchen. Food samples were from two different calorie levels (2000 kcal and 3000 kcal) of the two study diets. The entire daily meals (breakfast, lunch, dinner) for each of the two calorie levels of each study diet were collected, homogenized and then stored in freezers at -70^0C to await analysis on the selected day.

Woodson-Tenant Laboratories, Inc. in Dayton, Ohio was selected to

conduct laboratory analysis of the nutrient compositions of these food samples.

These analyses included moisture, total fat, protein, fiber, ash, calories (bomb

calorimeter), cholesterol, and fatty acid profile.

The methods of analysis for each component are as follows:

Fat	AOAC954.04
Fatty acid	AOCAS Ce-1e-01
Protein	AOAC 990.3
Fiber Crude	AOAC 962.09
Carbohydrate	AOAC 962.09
Ash	AOAC 923.03
Moisture, vacuum	AOAC 943.01
Cholesterol	AOAC 976.26
Bomb Calories	Parr Calorimeter

I-4 Data analysis

Difference in lipoprotein profiles were compared by using paried-t test. The

means of 3 measurements (one from week 5 and two of consecutive days of week

8) were used for the analysis. Data were analyzed using SAS program (Ver. 7.0). P

values less than 0.05 were considered to indicate statistical significant. All

significant levels were based upon two-tailed test.

II Results

II-1 Study participants and baseline Information

There were 13 men and 14 women who completed the feeding study. Thirty percent of the participants who completed the feeding study were Caucasian, fifty-six percent were Asian-Pacific islander, and 15 percent were mixed Asian and Caucasian (Table 2). The ages of the participants ranged from 20 to 52 years with the mean age being 32.5 years for men and 28.4 years for women (Table 1). Two were current drinkers or smokers (Table 3). Three females took birth control pills during the study period.

The body mass indices (BMI) ranged from 22.1 to 33.8 and from 18.2 to 28.5 for the males and females, respectively (Table 1). The baseline cholesterol levels ranged from desirable (<200 mg/dl [<5.2mmole/L]) to borderline high (200-239mg/dl [5.2-6.2mmole/L]) or high (≥240mg/dl [6.2mmole/L]) based upon the NCEP guidelines. For males, the baseline cholesterol ranged from 186 to 239.5 mg/dl and the baseline TG ranged from 47 to 310 mg/dl. For females, the baseline cholesterol ranged from 171 to 246 mg/dl and the baseline TG ranged form 39 to 171 mg/dl. The systolic blood pressure (SBP) for men and women ranged from 114 to 140 Hg and from 108 to 133 Hg, respectively. The diastolic blood pressure (DBP) ranged from 72 to 88 mm Hg for men and 60 to 96 mm Hg for women. Participants had normal blood pressure (SBP>140mm Hg, DBP>90mm Hg) to mild hypertension (SBP140-159mm Hg, DBP 90-99mm Hg). The males had

significantly higher levels of cholesterol (p=0.039), TG (p=0.0038) , and SBP (p=0.027) than the females in baseline. The randomization block by gender was successful in assigning participants into group 1 and group 2 since there were no significant differences in the age, BMI, cholesterol, TG and blood pressure in these two groups (Table 2).

Overall, there were no significant weight changes throughout the study periods. The mean, and its standard deviation, of the body weight changes as compared to their baseline weight was 0.22 ± 1.55 lbs. for men, and 0.4 ± 2.26 lbs. for women. Changes in SBP and DBP were not statistically significant, although both SPB (-0.96 ± 1.21 Hg) and DBP (-1.12 ± 0.86 Hg) tended to fall for those participants on the high monounsaturated fatty acids (HIMUFA) diet as compared to the typical American diet or the high saturated fatty acids (HISAT) diet. The diets were well accepted by the participants. The compliance was outstanding throughout the study periods as evaluated from the daily dairy, interviews and study monitors.

II-2 Food analysis

Table 5 shows comparisons between the analyzed mean for daily macronutrient, cholesterol and fiber intakes of the 12-day cycle menu at the 2,000 calorie level and the calculated nutrition profile using the Food Processor (ver Plus, 1994) and NDS (ver 2.92, 1997) software packages. Overall the differences

between the analyzed nutrient profiles and the calculated nutrient profiles were small except for the fiber content.

The percentage of calories derived from SFA and MUFA in the HISAT diet was similar for the calculated value and the analyzed value. The percentage of calories derived from total fat in the analyzed HISAT diet was significantly lower than the calculated HISAT diet, while the percentage of calories from PUFA was significantly higher in the analyzed HISAT diet than the calculated HISAT diet. The percentages of calories from both SFA and MUFA in the analyzed HIMUFA diet were significantly higher than the calculated HIMUFA diet. The percentages of calories from total fat as well as from PUFA were similar between the analyzed HIMUFA diet and the calculated HIMUFA diet. Daily dietary cholesterol in the analyzed HISAT diet was significantly lower than in the calculated HISAT diet.

Comparisons of fatty acid profiles between the analyzed HISAT diet and the analyzed HIMUFA diet are also shown in Table 5. The HIMUFA diet had a significantly higher percentage of calories derived form MUFA, but a lower percentage of calories derived from SFA than the HISAT diet. This difference was in accordance to the original study plan. The percentage of calories derived from PUFA was significantly lower in the HIMUFA diet than in the HISAT diet. The percentage of calories derived from total fat, as well as the daily dietary cholesterol levels, were comparable between the HISAT diet and the HIMUFA diet.

Analyzed daily calories, as well as analyzed fiber content, in both the

HISAT diet and the HIMUFA diet was significantly lower than calculated values.

The differences in analyzed fiber content between the HIMUFA diet and the

HISAT diet was statistically significant. There were no significant differences in

the analyzed daily calorie values between the two diets. Caloric data were derived

from analyzed carbohydrates, total fat, and protein based upon their Atwater

factors. Both the percentage of calories derived from protein and carbohydrates

were alike between the analyzed diets and the calculated diets except that there

was a significantly higher analyzed carbohydrate level than calculated

carbohydrate level in the HISAT diet.

As seen in Table 6, the calculated fiber content of each HIMUFA diet was

higher than of each HISAT diet except for weekend 3 since the HIMUFA diet

used whole nuts as one of the major fat sources. However, the differences between

the two analyzed study diets, as well as the comparisons between analyzed and

calculated data, were much greater than what was expected.

The individual fatty acid analysis confirmed the expected pattern of the

major fatty acids distribution for each study diet as seen in Table 7. The HISAT

diet had a significantly higher content of all saturated fatty acids than the

HIMUFA diet, which included Lauric acid (C12:0), Myristic acid (C14:0),

Palmitic acid (C16:0), and Stearic acid (C18:0). The HIMUFA diet had

significantly higher levels of monounsaturated fatty acids including Palmitoleic

acid (C16:1) and Oleic acid (18:1). There were no significant differences in the

content of Linoleic acid (C18:2) and Linolenic acid (C18:3) for the two study diets.

II-3 Diet effects on lipid profiles

Participant responses to the two experimental diets on plasma lipid profiles are shown in Tables 8. The HIMUFA diet significantly lowered plasma total cholesterol, LDL, HDL, and TG as compared to the HISAT diet for the overall group. These reductions were 11.6% (p<0.0001) in TC, 12.9% (P<0.0001) in LDL, 11.7% (p<0.0001) in HDL, and 6.9% (p<0.01) in TG of the HISAT diet, respectively. The differences between the diets in the VLDL were not significant (p=0.065) but tended to decrease in the HIMUFA diet. Substituting HIMUFA for HISAT created similar relative reductions in HDL and LDL levels, however these relative reductions resulted in little or no improvement in the LDL/HDL and Total cholesterol/HDL ratios. As seen in Table 9, LDL particle concentration (LDLpc) was significantly lower in the HIMUFA diet than the HISAT diet (11.8%, p<0.0001). This reflects that LDL particle numbers were reduced in conjunction with the lower concentration of LDL.

The response of lipid particle size and their sub-fractions from the participants to the diets are shown in Table 9, and Table 10, respectively. For the HIMUFA diet, a small but significant decrease occurred in both LDL and HDL particle size when compared to the HISAT diet. The reduction in the mean particle size of LDL and HDL was 0.16 nm (0.74%, p<0.005) and 0.10nm (1.08%,

p<0.001), respectively. These were due to reductions in the concentration of larger sub-fractions for both LDL and HDL. The difference in the mean particle size of VLDL was not significant during the study although it tended to be lower in the HIMUFA diet than in the HISAT diet (2.1%).

Although the mean of VLDL particle size was comparable between the two study diets, there were some significant changes in VLDL sub-classes in response to changes in dietary fat. As seen in Table 10, both Chylomicron (Chylos) (34.3%. P<0.005) and V3 (22.5%, p<0.005) were significantly lower in the HIMUFA diet than in the HISAT diet. There were no significant differences in the levels of IDL between the two study diets (p=0.33).

For LDL sub-fractions, there was a significantly lower level of L3 (27.6%, p<0.0001) for the HIMUFA diet as compared to the HISAT diet. In contrast, the levels of the smaller particles (L2 and L1) tended to be higher in the HIMUFA diet but these differences were not statistically significant. Among HDL sub-fractions, the larger particle- HDL_2 (H5+H4), and the concentrations of both H5 and H4, were significantly lower in the HIMUFA diet than in the HISAT diet. The differences in the smaller particle - HDL_3 (H3+H2+H1) was not significant, although H3 and H2 tended to increase while H1 tended to decrease in HIMUFA diet.

II-4 Validation between NMR and chemical measurement of lipid profiles

In Table 11, the dietary effects on lipid profiles using traditional chemical methods were shown to be very similar with the NMR method except for the TG lowering effect of the HIMUFA diet. This effect was more pronounced in the NMR than in the chemical measurement data. As seen in Table 12, the absolute concentration of total cholesterol, HDL, LDL and TG between NMR and the chemical method were all significantly different. Figure 1-4, shows that total cholesterol (r=0.71), LDL9 (r=0.74), HDL(r=0.98), and TG(r=0.98) using NMR were highly correlated with their concentration values using the chemical method from the regression analysis of the means of all measurements for each individuals.

TABLE 1: Baseline measurements- Study Population by gender

	Males (n=13)	Females (n=14)
Age (years)	32.5±9.9	28.4±6.7
BMI	26.0±3.2	22.1±3.2
Cholesterol (g/dl)	208.8±14.0	193.8±21.2
TG(mg/dl)	143.6±87.7	84.2±35.2
Systolic BP(mmHg)	124.6±8.1	117.3±8.0
Diastolic BP(mmHg)	82.0±5.2	78.2±8.3
Education:		
Undergraduate Student	7	8
Bachelor's Degree	0	2
Graduate Student	6	4
Housing:		
Off Campus	9	8
On Campus	3	6
Mixed	1	0

TABLE 2. Baseline measurements- Study population by group

	Group1 (HIMUFA-HISAT) (n=14, male=6)	Group2 (HISAT- HIMUFA) (n=13, male=7)
Age (years)	29.7±8.2	31.1±9.2
BMI	23.7±4.1	24.3±3.3
Cholesterol (mg/dl)	199.6±19.2	202.5±20.2
TG (mg/dl)	102.5±61.3	123.9±81.7
Systolic BP (mmHg)	120.8±10.5	120.8±6.9
Diastolic BP (mmHg)	79.4±5.2	80.7±9.0

TABLE3: Baseline Information - Study Population (Ethnicity)

	Males (n=13)	Females (n=14)	Percentage (n=27)
Caucasian	3	5	29.6
Chinese	1	4	18.5
Japanese	4	1	18.5
Korean	0	2	7.4
Asian Indian	1	0	3.7
Pacific Islander	1	0	3.7
Mixed	2	2	14.8
Filipino	1	0	3.7

TABLE 4: Baseline Information - Study Population (Social Habits)

	Males (n=13)	Females (n=14)
Drinking:		
Never	5	6
Current	7	6
Not current	1	1
Unknown	0	1
Smoking:		
Never	12	11
Current	1	1
Not current	0	2
Using Birth Control Pill:		
No	13	11
Yes	0	3

TABLE 5. Mean daily nutrient composition of the two study diets*

Variable	HISAT Diet		HIMUFA Diet	
	Calculated	Analysis	Calculated	Analysis
Energy (Kcal/day)	2000±0.4	1921±78[a]	2000±0.4	1941±65[a]
Fat (% of Kcal)	38±0	36.7±2[a]	38±0	38±2.2
SFA	20.4±2.9	19.5±2.6	7.8±0.5	8.5±0.5[a]
MUFA	8.5±0.5	9.3±2.5	22.4±0.5	24.2±1.3[a]
PUFA	6±0.6	6.5±0.9[a]	5.3±0.7	5.5±0.4[b]
Protein (% of Kcal)	15±0	14.5±1.1	15.0±0	15.1±1.5
CHO (% of Kcal)	46.9±0.3	48.8±2.6[a]	46.9±0.3	46.9±3.1
Cholesterol (mg/day)	300±0.3	268±27.8[a]	300±0.6	275±24.5
Fiber (g/day)	15.4±1.6	7.7±2.6[a]	16.3±1.4	11.7±5.3 [a,b]

* All value denotes Mean ± SD of the 12 days cycle menu
- a : p<0.05 (analysis vs. calculate)
- b: p<0.05 (HIMUFA diet vs. HISAT diet other than SFA and MUFA)

TABLE 6: Fiber content of daily menu of the two study diet

Menu	Analyzed Percentage		Analyzed Daily(g)		Calculated Daily	
	HISAT	HIMUFA	HISAT	HIMUFA	HISAT	HIMUFA
W1	0.4	0.5	5.86	7.33	13.30	14.40
W2	0.7	0.7	10.47	10.49	16.00	17.20
W3	0.4	0.7	6.37	10.93	17.30	17.30
W4	0.4	0.6	7.02	10.29	16.50	18.10
W5	0.5	0.6	8.57	10.12	13.80	15.80
W6	0.3	1.7	4.85	27.29	13.60	14.50
W7	0.4	1.0	6.11	15.12	16.20	17.40
W8	0.4	0.8	6.57	12.90	17.20	17.80
Wknd1	0.5	0.7	8.10	10.85	15.30	15.60
Wknd2	0.3	0.5	4.7	7.67	15.80	16.00
Wknd3	0.9	0.4	15.36	6.76	12.80	14.00
Wknd4	0.3	0.7	5.14	11.81	17.00	18.00

W1-W8 for the weekday
　　Wknd1-Wknd4 for the weekend

TABLE 7: Percentage of the major fatty acids in two study diets

Fatty Acid		HISAT Diet %	HIMUFA Diet %
SFA			
	C12:0	0.65±0.21	0.03±0.03
	C14:0	0.41±0.08	0.07±0.02
	C16:0	0.92±0.13	0.66±0.07
	C18:0	0.37±0.06	0.25±0.03
MUFA			
	C16:1	0.07±0.08	0.65±0.05
	C18:1	1.15±0.24	2.56±0.19
PUFA			
	C18:2	0.79±0.08	0.69±0.08
	C18:3	0.06±0.03	0.04±0.02

* All value denotes Mean ± SD of the weight percentage of the 12 days cycle menu

TABLE 8: Diet effects on plasma lipids by NMR - paired t test*

Lipids (mg/dl)	HISAT	HIMUFA	Difference (HIMUFA-HISAT)
Total Cholesterol	202.1±3.7	178.6±4.0	-23.5±2.6[¶]
LDL-C	127.1±3.6	110.5±4.1	-16.5±2.1[¶]
HDL	60.0±3.1	52.9±3.1	-7.0±1.3[¶]
Triglycerides	98.0±7.0	91.2±8.6	-6.8±2.8[‡]
VLDL	55.2±7.1	53.5±8.0	-1.7±2.4
TC/HDL	3.70±0.27	3.66±0.24	0.04±0.07
LDL/HDL	2.36±0.22	2.36±0.20	-0.001±0.07

* All value denotes Mean ± SEM of the mean of three measurements. One on week 5 and two on week 8
[¶] $p \leq 0.0001$, [¥] $p \leq 0.001$, [§] $p \leq 0.005$, [†] $p \leq 0.01$,[‡] $p \leq 0.05$,

TABLE 9: Diet effects on plasma lipoprotein size (nm) and particle concentration (nmole/L) by NMR– paired t test *

Lipoprotein	HISAT	HIMUFA	Difference (HIMUFA-HISAT)
VLDLps	43.41±1.06	42.78±1.23	-0.93±0.96
LDLps	21.55±0.08	21.39±0.10	-0.16±0.05[†]
HDLps	9.30±0.11	9.20±0.10	-0.10±0.03[§]
LDLpc	1297.9±39.8	1144.7±47.5	-153.2±22.6[¶]

* All values denote Mean ± SEM of the mean of 3 measurements. One on week 5 and two on week 8
[¶] p ≤0.0001, [¥] p≤0.001, [§] p≤0.005, [†] p≤0.01 ,[‡] p≤0.05,

TABLE 10: Diet effects on plasma lipoprotein subclasses by NMR- paired t test*

Lipoprotein(mg/dl)	HISAT	HIMUFA	Difference (HIMUFA-HISAT)
VLDL			
V7(Chylos)	1.66±0.19	1.09±0.19	-0.57±0.23[†]
V6	3.59±0.92	3.03±1.43	-0.56±1.06
V5	7.76±2.85	7.84±2.81	-0.08±0.80
V4	22.50±3.56	23.56±4.22	1.06±2.22
V3	9.90±1.21	7.67±1.17	-2.23±1.03[†]
V2	6.64±1.43	4.99±0.83	-1.65±1.02
V1	4.93±0.59	6.57±0.59	1.65±0.82
IDL/LDL			
IDL	5.77±1.11	6.18±1.23	0.40±1.11
L3(large)	89.81±5.34	65.06±5.51	-24.76±3.79[¶]
L2(intermediate)	26.19±6.25	32.81±7.45	6.63±3.52
L1(small)	5.32±1.57	6.52±1.60	1.20±1.12
HDL			
H5(HDL$_{2b}$)	9.81±1.73	7.92±1.36	-1.90±0.66[‡]
H4(HDL$_{2a}$)	30.67±2.48	24.75±2.42	-5.91±1.14[¶]
H3(HDL$_{3a}$)	6.90±1.35	7.36±1.51	0.46±0.60
H2(HDL$_{3b}$)	10.08±0.69	11.70±0.70	0.61±0.46
H1(HDL$_{3c}$)	1.59±0.40	1.28±0.33	-0.31±0.33

* All values denote Mean ± SEM of the means of 3 measurements. One on week 5 and two on week 8.
[¶] p ≤0.0001, [¥] p≤0.001, [§] p≤0.005, [†] p≤0.01 ,[‡] p≤0.05,

TABLE 11: Diet effects on plasma lipids - Chemical analysis*

Lipids(mg/dl)	HISAT	HIMUFA	Diet Effect
Total Cholesterol	215.6±4.0	191.7±3.8	-23.9±3.0[¶]
LDL-C	121.0±6.0	108.4±4.4	-12.9±3.7[§]
HDL	72.5±4.2	64.0±3.6	-8.5±8.9[¶]
Triglycerides	87.3±8.4	84.5±9.5	-2.7±2.8
Glucose	88.1±1.6	85.0±2.7	-3.1±3.3

* All value denotes Mean ± SE of the mean of 3 measurements. One on week 5 and two on week 8.
[¶] P≤ 0.0001, [§] p≤0.005

TABLE 12: Diet effects on plasma lipids - Chemical analysis vs NMR measurement

Lipids(mg/dl)		# Sample	Mean Difference (Chemical vs NMR)	P value (Pair t test)
TC		160	13.34±1.29	<0.0001
	Male	78	16.16±1.29	<0.0001
	Female	82	10.63±2.16	<0.0001
HDL		160	11.76±0.56	<0.0001
	Male	78	8.32±0.52	<0.0001
	Female	82	15.02±0.84	<0.0001
LDL		160	-3.01±1.49	0.0450
	Male	78	3.68±1.32	0.0068
	Female	82	-9.37±2.43	0.0002
TG		160	-8.52±12.55	<0.0001
	Male	78	-4.62±1.27	0.0005
	Female	82	-12.23±1.40	<0.0001

* Mean difference value denotes Mean ± SE mg/dl
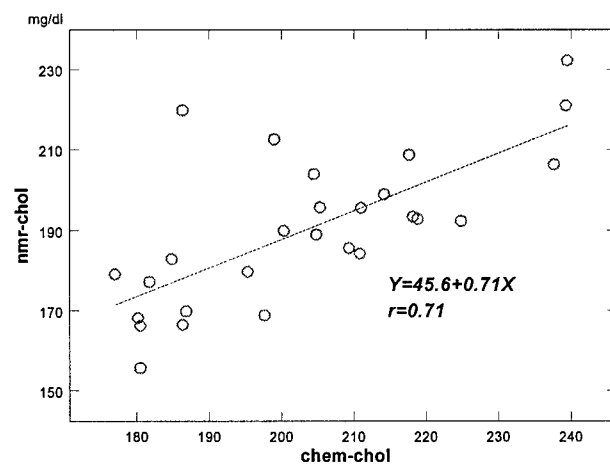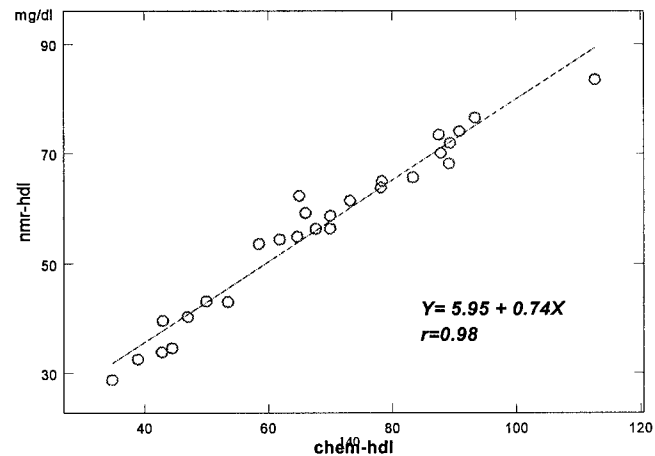
Fig1. Regression analysis of NMR-chol & chem-chol

Y=45.6+0.71X
r=0.71

Fig.2 Regression analysis of NMR-HDL & chem-HDL

Y= 5.95 + 0.74X
r=0.98

36

Fig3.Regression analysis of NMR-LDL & chem-LDL

$Y= 54.62 + 0.56X$
$r=0.74$

Fig4. Regression analysis of NMR-TG & chem-TG
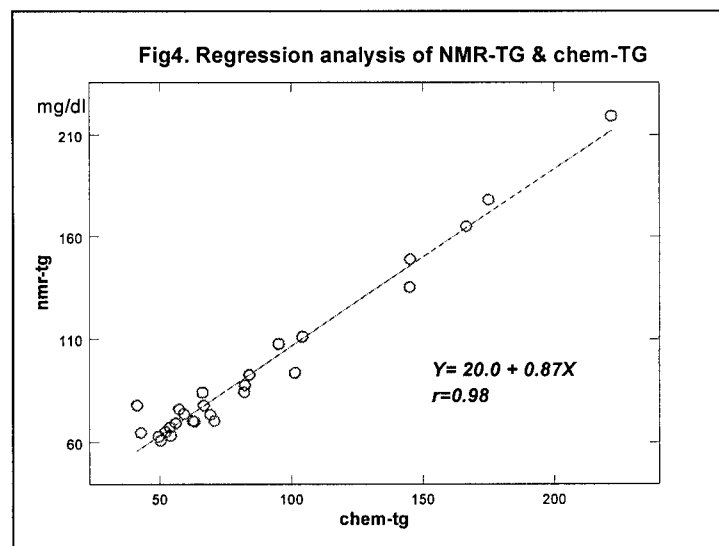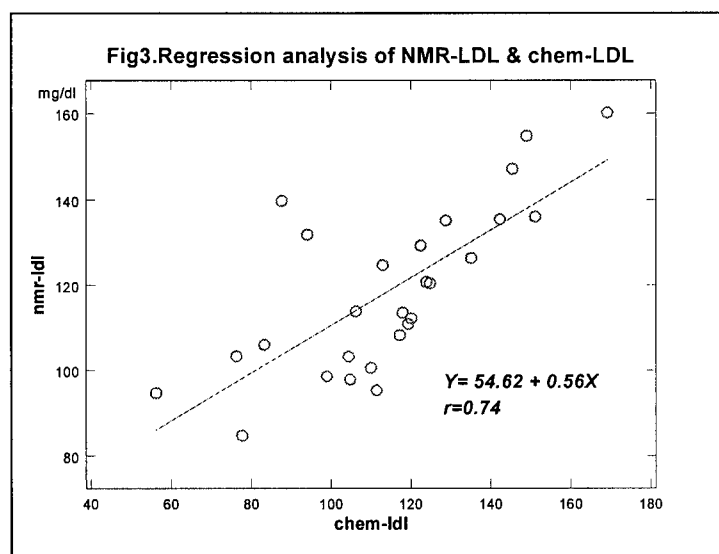
$Y= 20.0 + 0.87X$
$r=0.98$

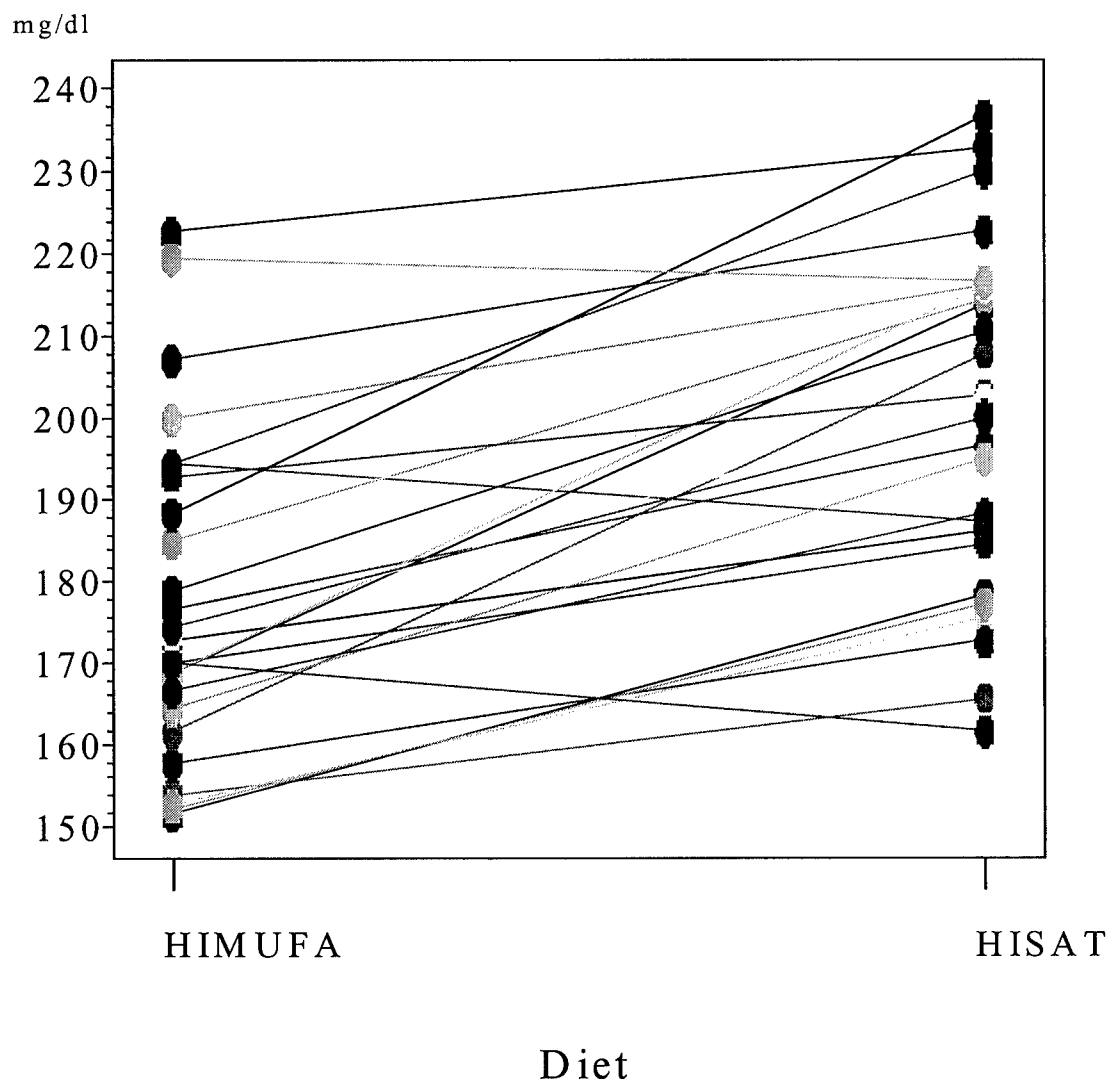# Figure 5. Individual cholesterol level responses to dietary fats

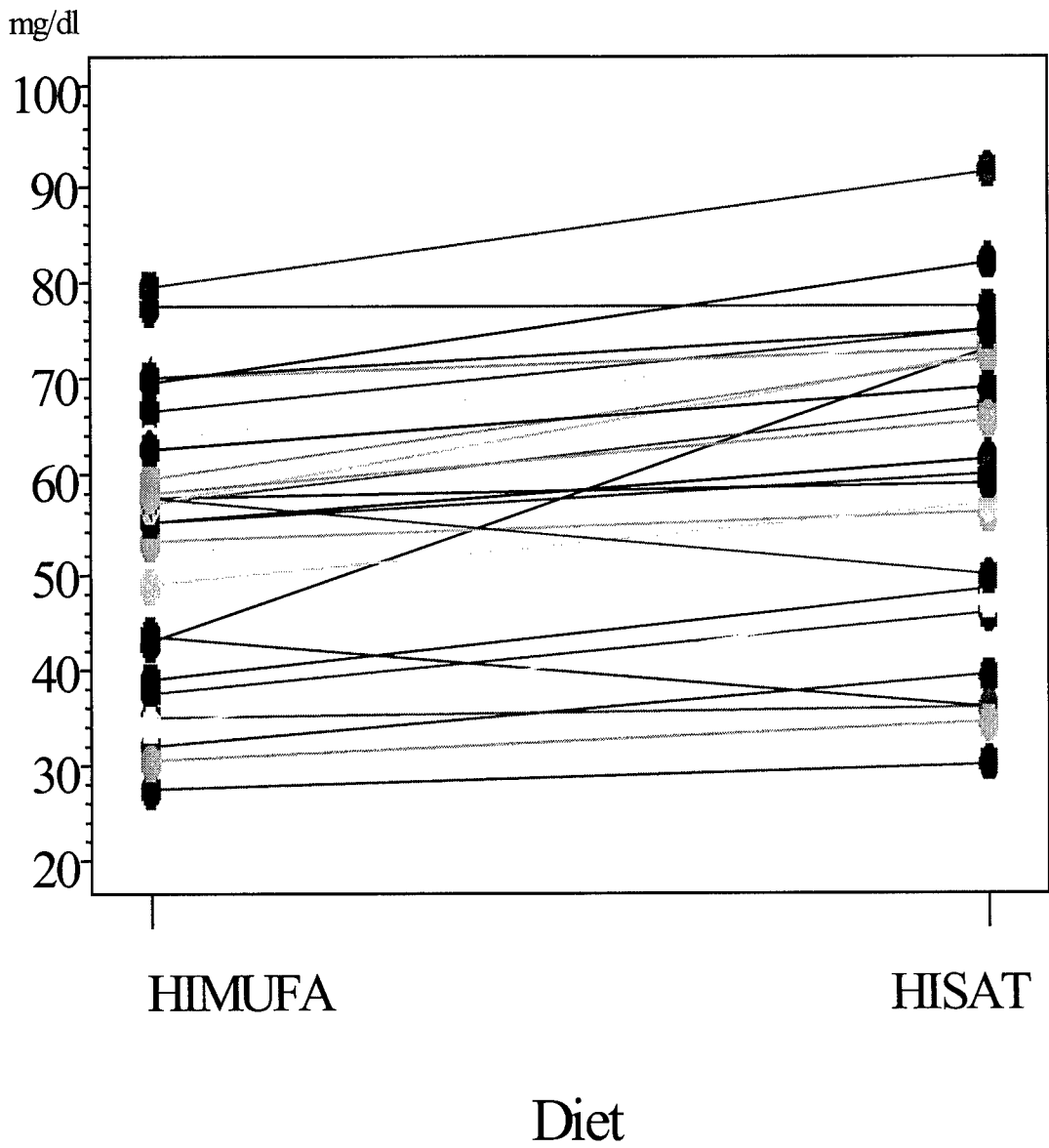# Figure 6. Individual HDL level responses to dietary fats

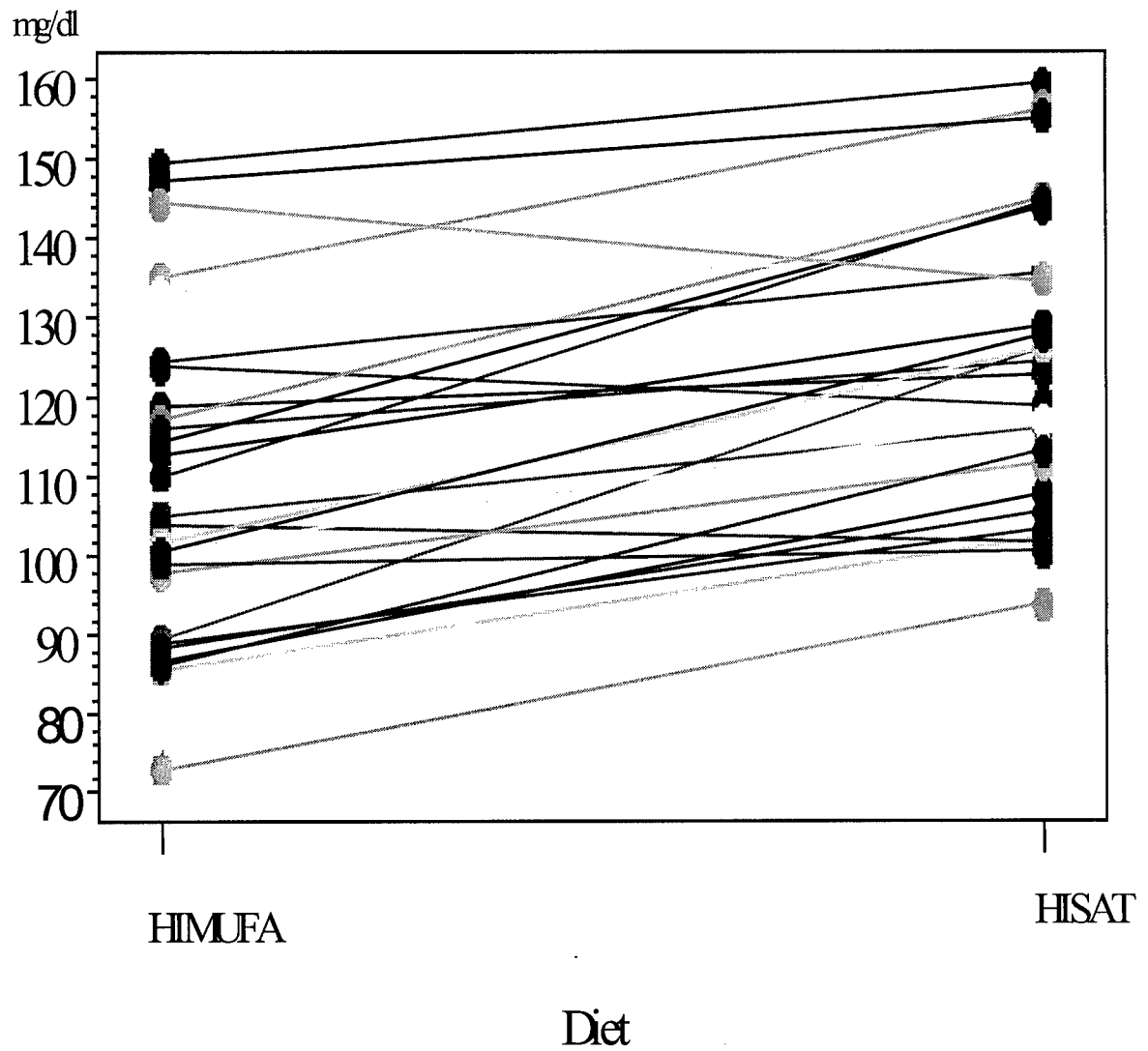# Figure 7. Individual LDL level responses to dietary fats

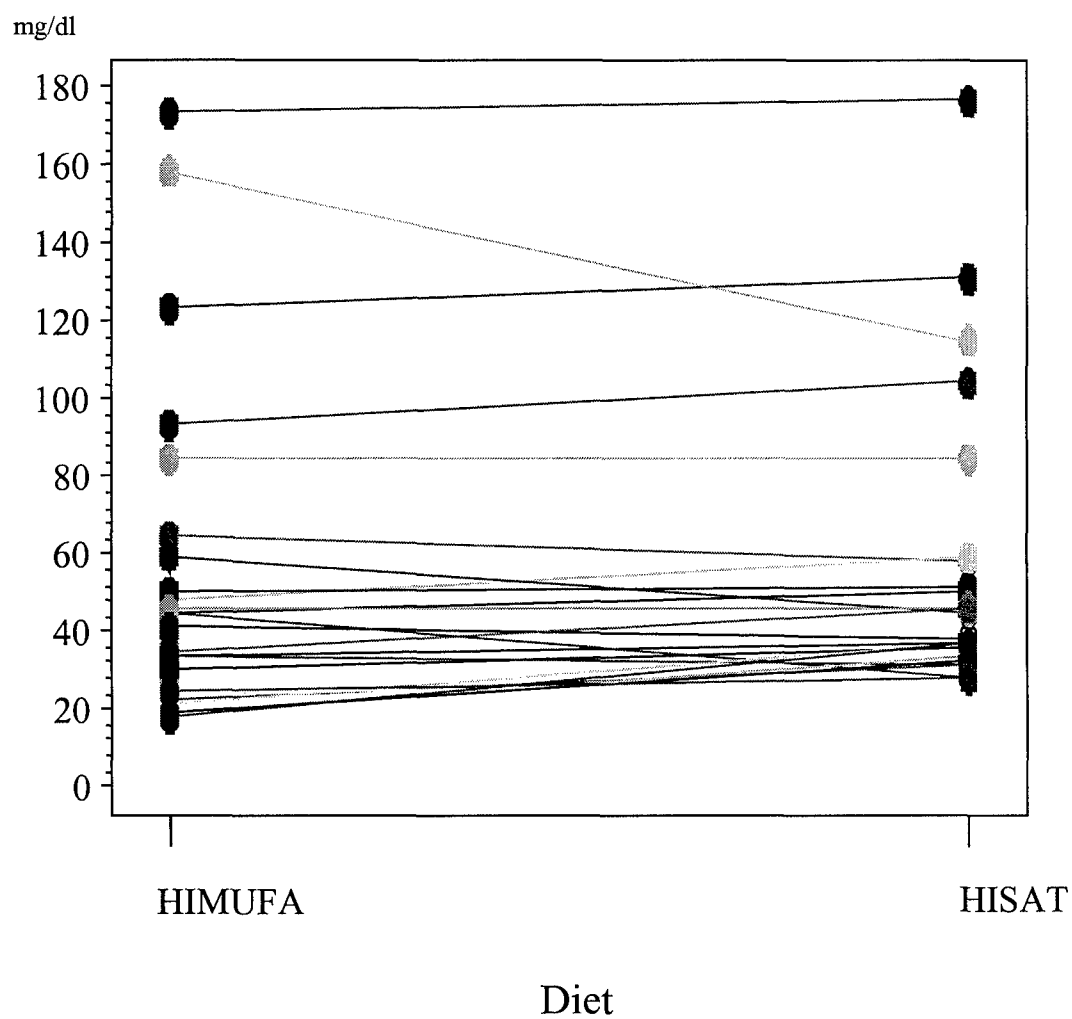Figure 8. Individual VLDL-tg level responses to dietary fats

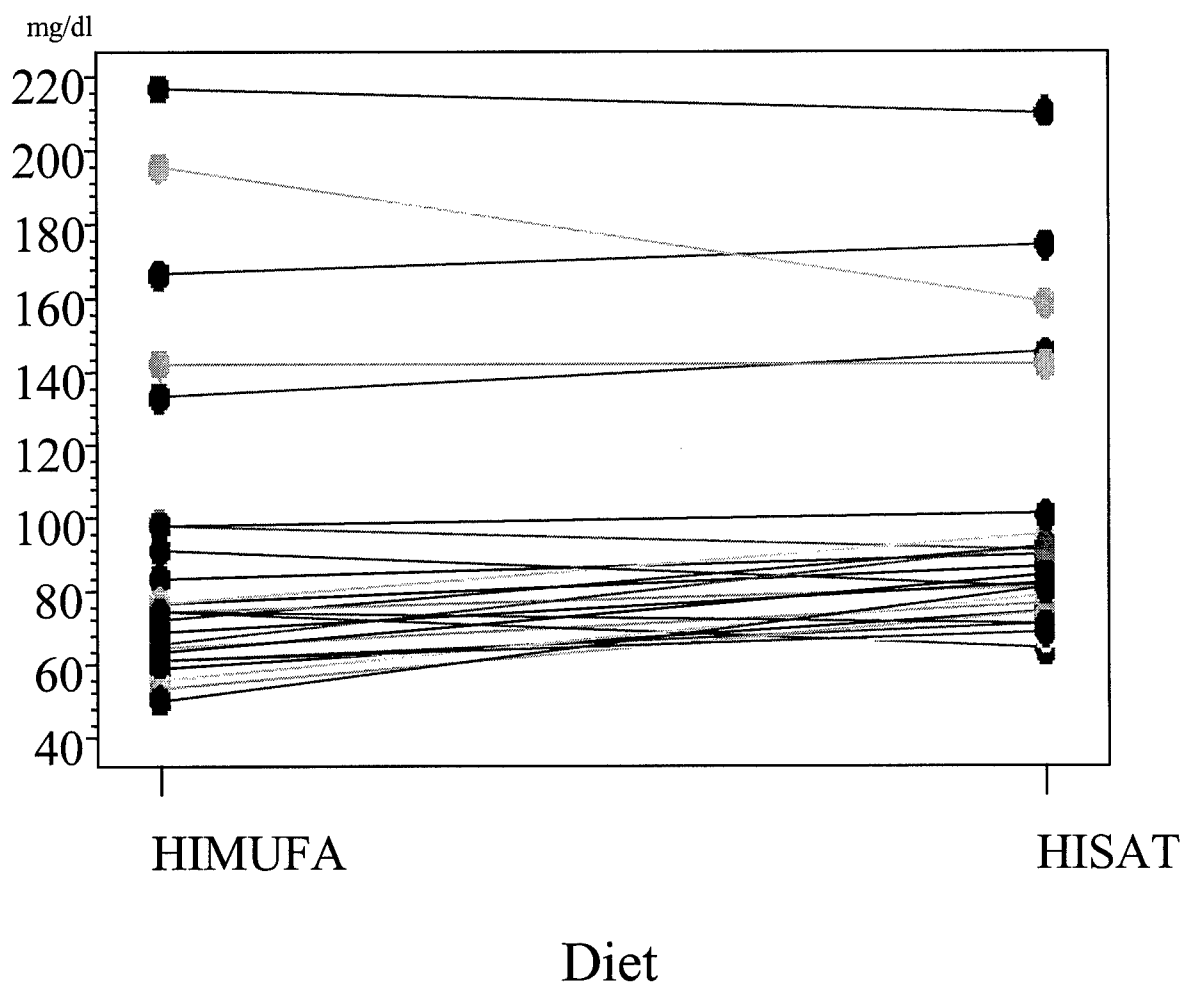# Figure 9. Individual TG level responses to dietary fats

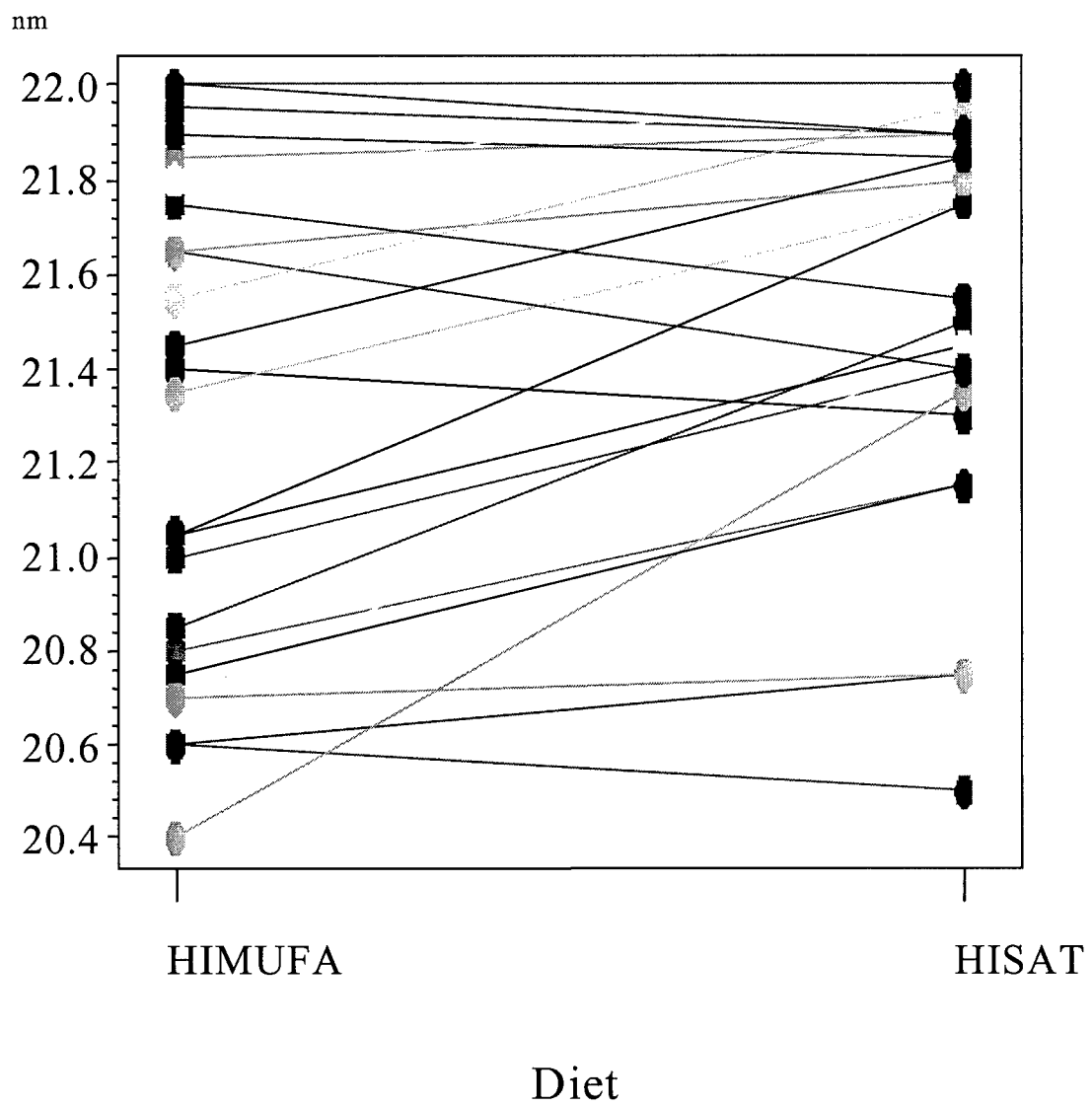# Figure 10. Individual LDL size responses to dietary fats

nm

43

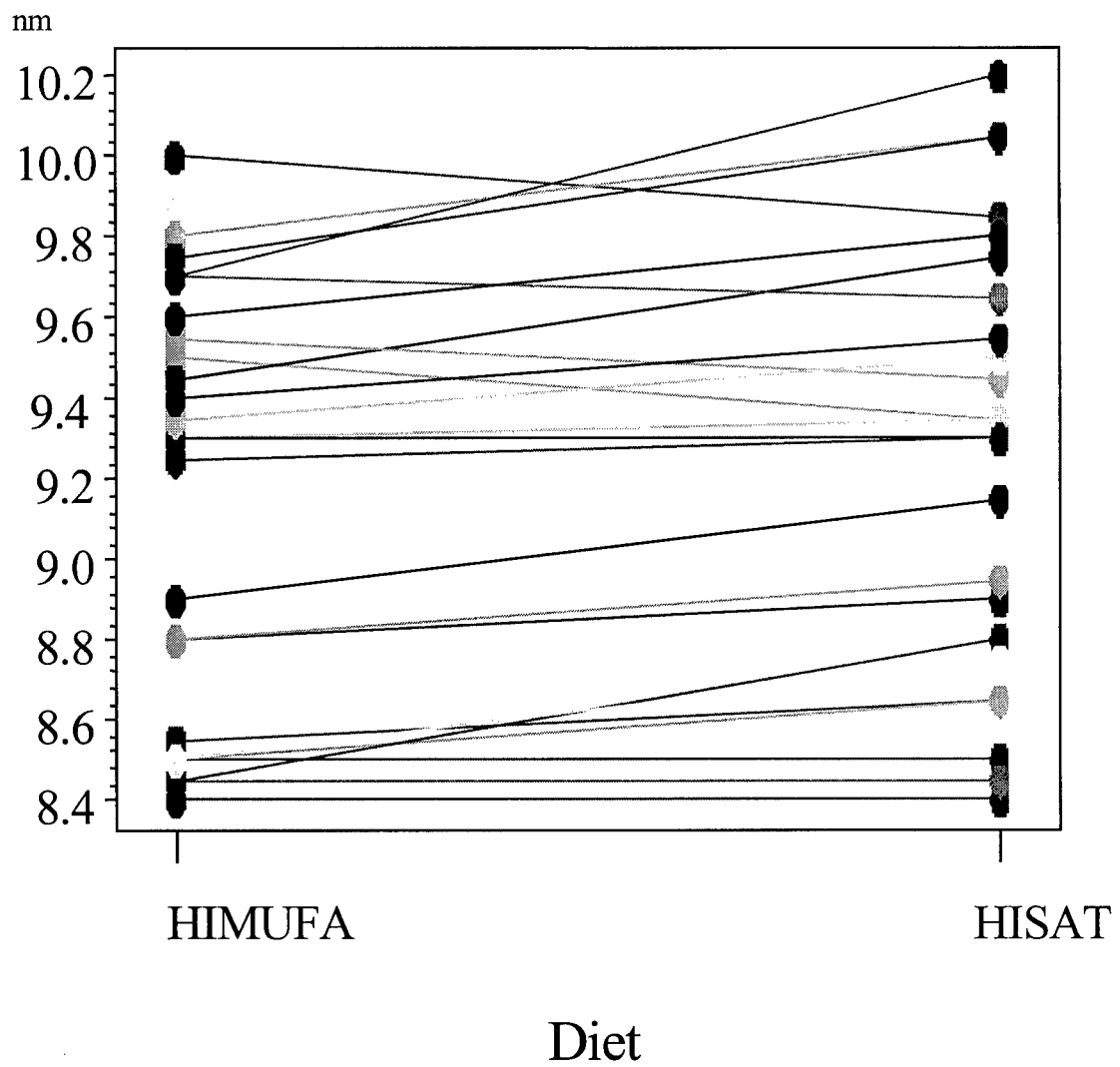# Figure 11. Individual HDL size responses to dietary fats

Figure 12. Individual LDL particle concentration responses to dietary fats
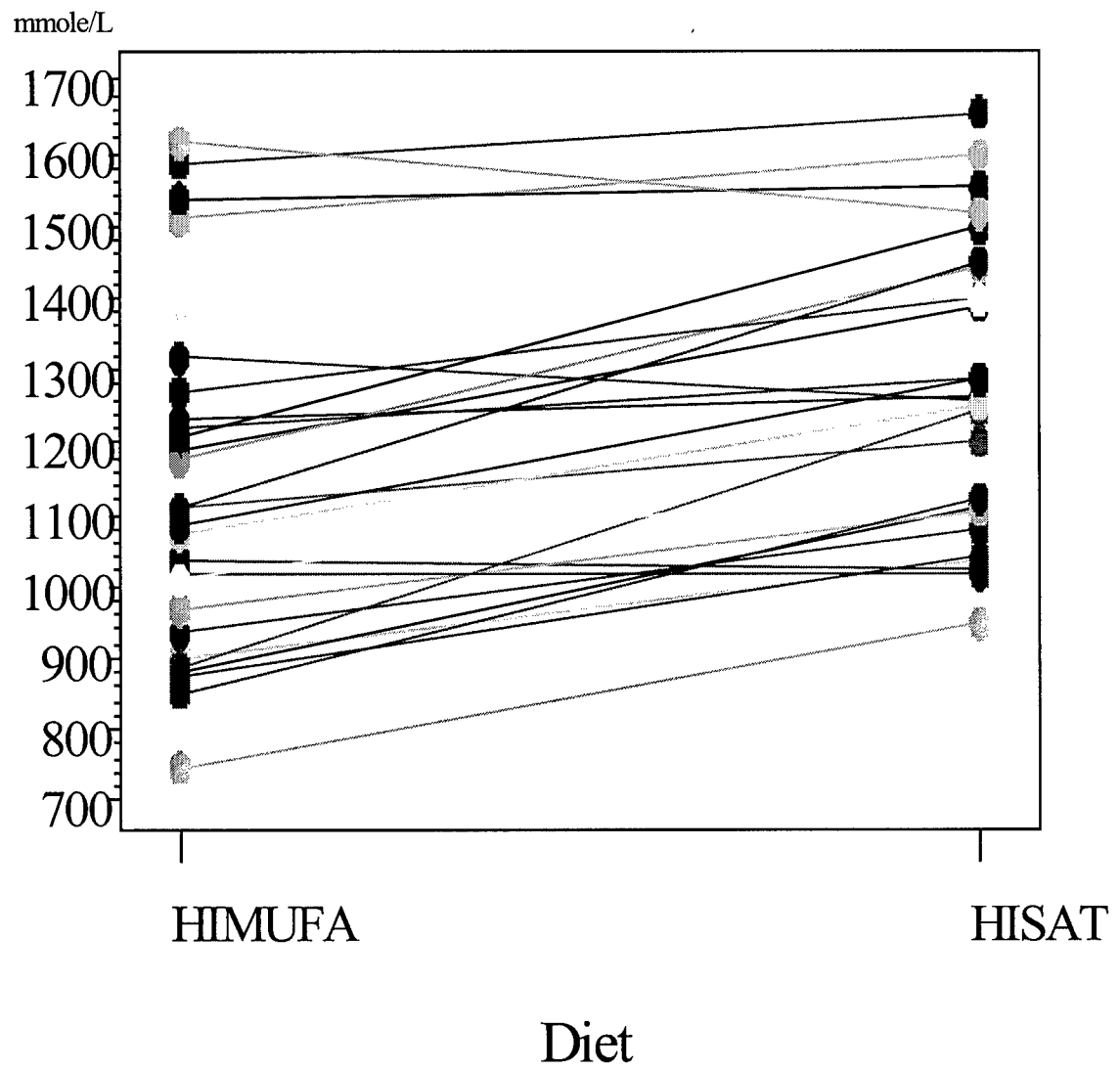
KEY RESEARCH ACCOMPLISHMENTS

- A high MUFA diet should be a more favorable replacement of SFA than a low fat diet in reducing cardiovascular risk based upon plasma cholesterol management.

- NMR is a valid and convenient tool to detect the lipoprotein profiles as new makers in assessment of cardiovascular disease risk.

- Macadamia nut and oil can be a good source for MUFA, since they have been very successfully incorporated into daily recipe and into high dense energy desserts. These types of foods can be developed so as to contribute to a healthy diet.

- Individual responds to dietary fat differently. Therefore, it is important to consider dietary modification by subpopulations such as gender or genetic factors.

REPORTABLE OUTCOMES

-Manuscripts, Presentations and Abstracts:

1. **Curb JD**, Wergowske G, Abbott RD, Dobbs JC, Tung KH, Austin M, Marcovina S, Waslien C. High monounsaturated fat macadamia nut diet effects on serum and lipoproteins. Presented at Experimental Biology 1998, California.

2. Curb JD, Waslein C, Wergowske G, Abbott RD, Austin M, Marcovina S, **Tung KH**. A high monousaurated fat (MUFA)- Macadamia nut diet and serum lipids and lipoproteins. Posted at University of Hawaii, School of Public Health 1st Annual Poster Session.

3. Waslien C, Curb JD, Wergowske G, Abbott RD, Dobbs JC, **Tung KH**, Austin M, Marcovna S. Posted at Hawaii Dietetic Association meetings in Honlulu, Hawaii 1998.

4. **Tung KH**. Clinical trial to determine the ability of a diet high in monounsaturated fatty acids to reduce risk factors for coronary heart disease. Presented at 1998-1999 University of Hawaii, School of Public Health Colloquium Series.

5. **Tung KH**, Waslien C, Elmer PJ, Abbott RD, Wergowske G, Curb JD. Long-term effects of diets high in monounsaturated fatty acid on plasma lipid levels in healthy men and women. The Macadamia Nut Study-Phase II. Presented at the Experimental Biology 1999, Washington DC.

6. **Tung KH,** Waslein C, Elmer PJ, Abbott RD, Wergowske G, Curb JD. Long-term effects of diets high in monounsaturated fatty acid on plasma lipid levels in healthy men and women. The Macadamia Nut Study, Phase II. Posted at Nutrition, Health & Healing in the New Miliennium of Hawaii Dietetic Association 1999, Honlulu.

7. **Tung KH**, Waslien C, Elmer PJ, Otvos JD, Wergowske G, Curb JD. Effects of diets high in monounsaturated fatty acids on plasma LDL subclasses in healthy men and women. To be presented at the Experimental Biology 2000, San Diego.

8. **Curb JD**, Wergowske G, Dobbs JC, Abbott RD, Huang B. Serum lipid effects of a high monounsaturated fat diet based on macadamia nuts. Arch Intern Med 2000;160:1154-1158.

-Degree obtained that is supported by this award:

Tung, Ko-Hui

Ph.D. in Biomedical Sciences (Biostatistics-Epidemiology) in May 2000

CONCLUSIONS

The current data strongly supports the beneficial effects of isocaloric substitution of saturated fatty acids with monounsaturated fatty acids, using a diet based on macadamia nuts and oil, can accomplish significant reductions in total and LDL cholesterol. These findings confirm the suggestion that the use of MUFA, instead of carbohydrates, as a substitution for SFA may be favorable for CVD risk. However, further investigations are needed to warrant the re-evaluation of CHD risk as associated with reductions in HDL cholesterol as well as in the particle sizes both in HDL and LDL in response to the dietary replacement of monounsaturated fat for saturated fat.

The significance of the reduction in LDL cholesterol, as well as LDL particle concentrations, in the HIMUFA diet is very promising. Though, the reduction in particle size, in particular the larger particles of LDL sub-fractions, seem to be unfavorable for the prevention of CVD risk based upon the evidence from various epidemiological studies. It is unclear whether small, dense LDL particles in a HIMUFA diet, would still enhance the disease risk in the same way that they do in a high saturated fat diet since the total LDL particle numbers were significantly reduced. In addition, LDL fatty acid composition is one of the important determinates for LDL's susceptibility to oxidation that may play a role in the pathogenesis of cardiovascular disease. Monounsaturated fatty acid in the diet can be incorporated into LDL fatty acid composition and can subsequently reduce susceptibility to oxidation in vitro. The protective effect of a high MUFA

diet, to a great extent, should reside in the small, dense LDL particle. It may be speculated that the enrichment of small, dense LDL particles with high MUFA would enhance its resistance to oxidative stress. Furthermore, LDL particle size, as well as small dense LDL, is not an independent predictor of CHD risk since the risk may also be impacted by insulin intolerance syndrome, which elevates plasma TG levels but lowers HDL cholesterol concentrations and LDL size. Common genes may exist and account for the interrelationship among these lipoprotein profiles and influences on individual CVD risk.

Although increased HDL levels in several trials have shown beneficial effects, the implication that lower levels of HDL concentration in conjunction with lower levels of LDL and triglycerides in response to a high-monounsaturated diet may be correlated with an increase in CHD risk may be unfounded. Lower levels of HDL cholesterol caused by a HIMUFA diet may be offset by significant reductions of LDL cholesterol. Most importantly is that while HDL levels are reduced there may be no changes in the reverse cholesterol transport function of HDL in high MUFA diets. The relevance of anti-artherogenic actions of HDL subfractions, as well as the role of HDL in the transporting and clearance of plasma lipid hydroperoxides still remains unclear. A primary or secondary prevention trial like the Lyon Diet Heart study may address the specific questions of the effects of high monounsaturated diet induced reductions in HDL, particularly in regards to HDL_2, on cardiovascular disease risk.

On the basis of plasma lipoprotein responses in this and previous studies, it is prudent at this point of time to recommend that MUFA can be a good alternative for SFA in the diet. A diet that provides up to 15% of calories form MUFA, meets the dietary guidelines of NECP (≤30% fat, 8% SFA) for the general public. A diet that is higher in MUFAs (16-22% of calorie), like the current study, could be an optimal strategy in improving upon the poor adherence of a low fat diet and cholesterol control, as long as daily energy balance and constant body weight is achieved.

The impact of the changes in other potential atherogenic factors in response to diets that are high in monounsaturated fat diet, such as Lp(a), Factor VII ,and genetic factors, should also be considered. A better understanding of the effects of these changes would be worth the effort as part of an overall investment into the research of the mechanisms of metabolic traits and postprandial states, as well as the artheropathogenesis among lipids and lipoproteins in dietary interventions. It not only can help us to evaluate and confirm the significance of the relationship between dietary fat modification and coronary heart disease but also to help establishment long-run public health strategies and policies for coronary heart disease prevention.

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APPENDICES:

List of all personnel who received pay from the contract

Name		Job Title
(Last name,	**first name)**	**Job Title**
Baldino,	Ruth	Recruiter
Bonilla,	Benecito	Cook helper
Campos,	Violet	Cook helper
Dibas,	Chester	Cook
Domdom,	Dinna	Project Coordinator
Duldulao,	Lolito	Cook
Flint,	Mary	Cook
Franklin,	Buddy	Cook helper
Hein,	Evelyn	Project Coordinator
Hsia,	Liang-ho	Cook helper
Jardine,	Sunny	Dishwasher
Kane,	Rod	Cook
Monje,	Sanny	Cook helper
Nakagawara,	Linda	Cook helper
Nakamura,	Troy	Cook
Nakata,	James	Cook
Nicholson,	Diane	Phlebotomist
Pacis,	Ceasar	Cook
Poon,	Sau-ling	Cook helper
Rabanal,	Ofelia	Lab Tech.
Resgonia,	Daryn	Cook
Richards,	Allison	Lab Tech.
Sagon,	Dionicio	Baker
Shigeta,	Sheryl	Lab Tech.
Takamoto,	Derek	Head Cook
Thomas,	Dale	Cook
Tung,	Ko-hui	Nutritionist/Epidemiologist

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POSTPRANDIAL LIPEMIA EFFECTS OF FAT FROM WHOLE ALMONDS VERSUS ALMOND OIL. Dees PA, Rock CL, Freeman LR, Schneeman, BO. Depts of Nutrition & Med., Univ of California, Davis, Davis, CA 95616

Altered postprandial lipemia is increasingly recognized as an important heart disease risk marker. The packaging or metabolism of fat with other dietary ingredients in foods, meals is likely to alter its digestion, absorption with subsequent effects on postprandial lipoprotein metabolism and ultimately on heart disease risk. We set out to determine if provision of fat as whole almonds compared to almond oil changes the postprandial response to an acute test meal. Using a crossover design, normolipidemic adult subjects (n=14,M=8,F=6) consumed in random order 3 isoenergetic test meals at least 1 week apart. Test meals contained 30% energy from fat, of which >2-3 was from either whole almonds (AWL), almond oil (AOL) or control oil (CRL). After an overnight fast, subjects had a blood sample drawn (Tzero) and then consumed the meal within 20 minutes. Further samples were drawn at 90, 120, 180, 240, 300 and 360 minutes. Statistical analysis (repeated measures ANOVA) of the postprandial triglyceride (TG), expressed as increments to adjust for differing Tzero levels, indicated that differences by meal approached significance (p<0.06) while time effects and meal*time interactions were highly significant (p<0.009 & p<0.001, respectively). Plotting showed that AWL had a significantly delayed TG rise at the early time points compared to both AOL and CRL while no differences were observed between AOL and CRL. These data suggest that dietary fat ingestion as whole almonds significantly affects its absorption and subsequent postprandial lipid/lipoprotein metabolism. Funded by the Almond Board of California.

2940

FREQUENT NUT CONSUMPTION AND RISK OF CORONARY HEART DISEASE: THE NURSES' HEALTH STUDY F.B. Hu, M.J. Stampfer, J.E. Manson, E. Rimm, G.A. Colditz, B. Rosner, F.J. Speizer, C.H. Hennekens, W.C. Willett. Harvard University. Boston, MA

Objective. To investigate the relation of nut consumption to risk of coronary heart disease (CHD). **Methods.** We examined the association between nut consumption and incidence of CHD in a cohort of 84,409 women 34 through 59 years of age and without previously diagnosed CHD, stroke, or cancer in 1980. Nut consumption was assessed at baseline and updated periodically during follow-up using validated dietary questionnaires. We documented 1255 major coronary disease events (861 nonfatal myocardial infarction (MI) and 394 fatal CHD) during 14 years of follow-up. **Findings.** Compared to women who rarely ate nuts (never or < once a month), those with frequent consumption (5+ times week) had significantly lower risk of total CHD (RR = 0.65, 95% CI: 0.47-0.89, p for trend = 0.0009) after adjusting for a wide range of CHD risk factors. The magnitude of risk reduction was similar for fatal CHD (RR=0.61, 0.35-1.05, p for trend = 0.007) and nonfatal MI (RR=0.68, 0.47-1.00, p for trend = 0.04). This inverse association was independent of smoking, alcohol use, multivitamin and vitamin E supplement use, body mass index, exercise, and intakes of vegetables or fruits. **Conclusions.** Frequent nut consumption was associated with reduced risk of CHD.

2941

EFFECTS OF PEANUTS ON HUNGER AND FOOD INTAKE IN HUMANS. R.D. Mattes and S.K. Voisard. Purdue University, W. Lafayette, IN 47907.

Epidemiologic studies indicate regular consumption of peanuts does not promote weight gain and is inversely related to coronary heart disease risk. This intervention study determined the effects of a 500kcal peanut preload on hunger and food intake in 12 male and 12 female, normal weight adults. To identify factor(s) associated with outcome measures, responses were also monitored to randomly presented isoenergetic loads of peanut butter (rheology control), almonds (tree nut), chestnuts (macronutrient control), chocolate (sensory control) as well as pickles (matched on weight), rice cakes (matched on volume) or no load (time control) at one week intervals. A statistically significant and comparable reduction in hunger was observed for all isoenergetic loads while weight, volume and time controls lead to no immediate decline and a significant elevation at 3 hours relative to baseline. Total energy intake was comparable across treatments and relative to baseline. Mean total daily fat intake was significantly higher following the peanut, peanut butter, almond and chocolate loads with the fatty acid composition reflecting the content of the loads. In summary, peanuts have a strong satiety value due to their high energy content, elicit dietary energy but not macronutrient compensation and promote ingestion of a diet with higher proportions of mono- and polyunsaturated fat.

Supported by U.S. AID grant #LAG-4048-G-00-6013-00; Subgrant #RD309-022/4092094 (Peanut Collaborative Research Support Program)

2942

EFFECTS OF WALNUTS ON THE SERUM LIPID PROFILE OF HYPERCHOLESTEROLEMIC SUBJECTS: THE BARCELONA WALNUT TRIAL. D. Zambón, B. Campero, A. Pérez-Heras, C. Rodríguez-Villar, E. Ros, E. Casals, S. Muñoz, J.C. Laguna, J. Sabaté. Lipid Clinic, Nutrition & Dietetics Serv., and Clin. Biochem. Serv., Hospital Clínic, Barcelona Sch. of Med.; D. Pharmacology, Barcelona Sch. of Pharmacy, Spain, and D. Nutrition, Loma Linda Univ., CA, USA.

Cardiovascular health benefits are associated with the consumption of walnuts. One reason could be the favorable effect on plasma lipids, as shown in normolipidemic subjects (N Engl J Med 1993;328:603-7). We assessed the effect of walnuts on serum lipids in hyperlipidemic subjects. In a randomized, cross-over study, 49 subjects (23 women, 26 men; mean age 56 yrs, range 34-68) with primary hypercholesterolemia [mean values in mg/d: total cholesterol (TC) 278, low-density lipoprotein cholesterol (LDL-C) 193, high-density lipoprotein cholesterol (HDL-C) 56, triglycerides (TG) 141] received two isocaloric diets, containing identical macronutrients, but differing in fatty acid (FA) content: a monounsaturated FA (MUFA) diet, olive oil-rich (MO), and a polyunsaturated FA (PUFA) diet, containing ~50 g walnuts day (PW). Respective fat composition values (percent of daily energy) were: total fat 30 vs 33, saturated FA 5 vs 5, MUFA 21 vs 16, and PUFA 4 vs 12. The main changes in the PW diet with respect to the MO diet were a 150% increase in 18:2n-6 and a 300% increase in 18:3n-3. After 6 wks. on each diet, blood was obtained for serum lipoprotein analysis. TC, LDL-C, and apolipoprotein B levels decreased 10% each (p<0.001) after the PW diet in comparison with the MO diet. The effects were similar in men and women. In conclusion walnut consumption favorably modifies the plasma lipid profile in hypercholesterolemic subjects. Supported by the Walnut Comission of California and Fundació Privada Catalana de Nutrició i Lípids.

2943

HIGH-MUFA DIETS WITH PEANUTS-PEANUT BUTTER (P PB) OR PEANUT OIL (PO) LOWER TOTAL CHOLESTEROL (TC) AND LDL-C IDENTICALLY TO A STEP 2 DIET BUT ELIMINATE THE TRIGLYCERIDE (TG) INCREASE. T.A. Pearson, T.D. Etherton, K. Moriarty, R. Reed and P.M. Kris-Etherton. Penn State Univ, Univ Park, PA 16802, Univ. Rochester School of Med, Rochester, NY 14620, Bassett Res Inst, Cooperstown, NY 13326

To determine whether the lipid lowering effects of diets high in MUFA from P PB or PO are comparable to those of diets high in MUFA from olive oil (OO), we compared the effects of five different diets on serum lipids in 22 healthy adults (9 men and 13 women, age 21-54). A randomized, double-blind, five-period crossover design was used to evaluate the following diets: average American (35% fat, 15% SFA), low-fat (25% fat, 7% SFA), OO (35% fat, 6% SFA), P PB (35% fat, 7% SFA), and PO (35% fat, 7% SFA). Subjects were provided all foods and beverages for each 25 day diet period and fasting blood samples were drawn twice during the final week of each diet period. Lipid profile data are summarized:

	AA	Low-Fat	OO	P/PB	PO
TC	210 ± 9ᵃ	190 ± 9ᵇ	185 ± 9ᵇ	187 ± 9ᵇ	191 ± 9ᵇ
LDL-C	137 ± 8ᵃ	116 ± 8ᵇ	115 ± 8ᵇ	117 ± 8ᵇ	121 ± 8ᵇ
HDL-C	58 ± 6	46 ± 6	49 ± 6	47 ± 6	48 ± 6
TG	118 ± 12ᵃ	131 ± 12ᵃ	102 ± 12ᶜ	103 ± 12ᶜ	105 ± 12ᶜ

means with different superscripts differ at p < 0.05

In summary, OO, P PB and PO can be used interchangeably in high-MUFA low-SFA diets, creating additional diet planning options for the development of diets designed to lower TC and LDL-C. Moreover, these diets are all superior to low-fat low-SFA diets because they do not elevate TG. Funded by The Peanut Institute.

2944

High Monounsaturated Fat Macadamia Nut Diets: Effects on Serum Lipids and Lipoproteins J.D. Curb, G. Wergowski, R.D. Abbott, J.C. Dobbs, J. Tung, M.A. Austin, S. Marcovina, SPON C. Washer. Univ. of Hawaii. Honolulu HI 96813

Macadamia nuts have a fatty acid profile which differs from most common sources of monounsaturated fatty acids in the diet. In order to investigate one of the few naturally occurring foods, and the only nut, which has a relatively high proportion of palmitoleic acid a multiphase study was conducted. First, in a randomized crossover design feeding study 30 volunteers 18 to 35 years old were fed 1 of 3 diets for 30 days:Macadamia (MAC)(37% fat kcal,FAT, 9%saturated fat-kcal,SAT), an AHA Step 1 diet (AHA)30%FAT, 9%SAT), or a typical US diet (HISAT)37%FAT, 15%SAT). Fasting cholesterol, HDL, triglycerides, apolipoproteins A-I(Apo A-I) and A-II(Apo A-II), lipoprotein [Lp(a)], and LDL peak particle diameter (LDL-PPD) were measured on 3 consecutive days at the end of each diet period. Overall, cholesterol was 5% lower on MAC(191 mg/dl) than on HISAT (201 mg dl) diets(p<0.05), as were both LDL (7.5%, p<0.05) and HDL(3.6%, p<0.01). AHA and MAC effects were similar. In contrast, triglycerides were lower on MAC than on AHA (10%, p<0.05). Lp(a) was higher and LDL-PPD, Apo A-I, and Apo A-II lower in the MAC and AHA (p<0.05). Although all feeding studies are subject to large variability, trends among the six blocks used for randomization suggested that a longer feeding was needed to show MAC full effect. Preliminary results from a second 17 week feeding study with MAC and HISAT will be presented.

431.7

FERRITIN RECEPTORS IN THE BRAIN

S Hart, S Powers, J Connor. Departments of Neuroscience & Anatomy and Neurosurgery, M.S. Hershey Medical Center, Hershey, PA 17033

Traditionally, transferrin has been considered the primary iron delivery protein to the brain. However, transferrin receptors are expressed in gray matter whereas the majority of iron is found in white matter. We have recently established that ferritin receptors are expressed in the brain and are selectively found in white matter tracts. Thus, the distribution of ferritin receptors in brain is exactly opposite that of transferrin receptors. The distribution of ferritin receptors in white matter occurs in both rodent and human brains and ferritin receptors are selectively expressed on oligodendrocytes in cell culture. In Multiple Sclerosis (MS), the prototype of demyelinating diseases, ferritin receptor expression in the periplaque regions is lost and replaced by transferrin receptors. In a developmental study on mice, the presence of ferritin receptors in white matter coincides with the onset of myelination and, we propose, the disappearance of transferrin receptors from white matter. The expression of ferritin receptors is consistent with the notion that iron requirements are significant and continuous for myelination and indicate that ferritin, not transferrin, is the predominant iron delivery protein to maintain myelin production.

EFFECTS OF NUT CONSUMPTION ON CHD RISK AND BODY WEIGHT (432.1-432.4)

432.1

Impact of consuming peanuts and peanut products on energy and nutrient intakes of American adults.
B Eissenstat, V Juturu, G Hsieh, D Maddox, PM Kris-Etherton. Dept. of Nutrition. The Penn State University, Univ. Park, PA 16802

The impact of consuming peanuts and peanut products on the energy and nutrient intakes of free living male and female adults (>20 years) relative to non-users was assessed using data reported in the Continuing Survey of Food Intake by Individuals CSFII from 1994-1996. Peanut use was subdivided to identify how peanuts were consumed ie. peanut butter, whole peanuts, part of a meal, savory or sweet snacks; and relative consumption high, moderate, low). 24% of CSFII respondents (males, n=980 and females, n=833) consumed peanuts or peanut products; 13% consumed peanuts as peanut butter; 9% as a sweet snack; 3% as a savory snack; and 1.7% as peanuts. Macro and micro nutrient analysis identified highly significant differences (P<0.001) between peanut users and nonusers. Peanut users tended to achieve higher RDAs for micronutrients and had a higher fiber content than nonusers. A "Mean Adequacy Ratio" was calculated as a measure of the overall nutrient profile of the diets and was significantly greater for peanut users (men.91.5;women.85.7) compared to nonusers (men.86.2; women.81.2). Percent of energy from MUFA was slightly higher in peanut users (men. 13.8%; women. 13.1%) than nonusers (men. 13.0%; women. 12.5%) but, percent of energy from saturated fat was comparable for users and nonusers of both sexes. Energy intake was higher in peanut users however, overall diet quality was greater. (Funded by the Peanut Institute)

432.2

Nut consumption and risk of recurrent coronary heart disease
L. Brown, B. Rosner, W.C. Willett, F.M. Sacks. Harvard School of Public Health, Boston, MA

Recent epidemiologic and clinical evidence suggests that nuts may reduce the risk of coronary heart disease (CHD) despite their high fat content. We examined the relation between frequency of nut consumption and risk of recurrent CHD in a population of post-myocardial infarction (MI) men and women aged 21-75 years (mean 59 years) with total cholesterol >240 mg/dl (mean 209 mg/dl). Nut consumption was assessed at baseline using a well validated semiquantitative food frequency questionnaire. We documented 323 nonfatal MIs and coronary deaths during 4.2 years of follow up. Compared to those who rarely ate nuts (never or less than once per month), those with more frequent consumption (2 or more servings per week) had a significantly lower risk of total CHD (RR=0.75, 95% CI: 0.49-1.15; P for trend=0.03) after adjusting for age, smoking and other known CHD risk factors. We investigated nutrients that could explain the possible beneficial association of nuts with CHD. Unsaturated fatty acids, minerals, and antioxidant vitamins were not significantly associated with CHD, and adjusting for these nutrients did not materially alter the results. Our findings, together with other epidemiologic and clinical studies support a role of nuts in protecting against recurrent CHD

432.3

ISOCALORIC REPLACEMENT OF 20% ENERGY ON A STEP I DIET WITH PECANS IMPROVE THE LIPID PROFILE OF HEALTHY MEN AND WOMEN. J Sabate, S Rajaram, K Stote Loma Linda University, Loma Linda, CA 92350

Objective. To determine the effect of pecans on blood lipids when replacing 20% of energy in a NCEP Step 1 diet Methods 24 healthy subjects (14 men and 10 women, age 25-55) in a carefully controlled metabolic study were fed a western-type diet for 2 weeks (baseline) and then randomized to a control diet (Step 1) or pecan diet (80% of energy from the Step 1 diet, plus 20% of energy from pecans) These diets were administered for 4 weeks in parallel design Blood samples were drawn twice during the final week of each period and analyzed for blood lipids

Results*.

	Baseline Values		Changes from Baseline†	
	Step 1	Pecan	Step 1	Pecan
T-Cholesterol, mg/dL	193±36	198±30	-5±10	-20±18†
LDL-C, mg/dL	122±28	125±22	-5±8	-17±13†
HDL-C, mg/dL	51±10	49±9	-2±4	-4±3
LDL/HDL Ratio	2.5±.8	2.7±.7	-.03±.17	-.34±.19†
Triglycerides, mg/dL	100±63	120±57	8±28	-13±42

* mean±SD † p value <.05

Conclusions. The incorporation of pecans for 4 weeks to a NCEP Step 1 diet without changing total energy intake lowered total serum cholesterol, LDL-cholesterol and triglycerides and markedly improved the lipoprotein profile of healthy men and women Funded by National Pecan Shellers Association

432.4

LONG-TERM EFFECTS OF DIETS HIGH IN MONOUNSATURATED FATTY ACID ON PLASMA LIPID LEVELS IN HEALTHY MEN AND WOMEN
The Macadamia Nut Study, Phase II
KH Tung, C. Washen, P.J. Elmer, R.D. Abbott, G Wergowske, J D Ca Univ of Hawaii, Hawaii HI 96822, Univ. of Minnesota, Minneapolis, MN 55454, Univ. of Virginia, Charlottesville, VA 22908

A randomized crossover feeding trial with a high monounsaturated fat (HIMUFA) based on macadamia nuts and oil and a typical American diet high in saturated fat (HISAT) was conducted on 27 healthy men and women aged 20 to 52. Fatty acid profiles for the 2-diets were: HIMUFA 38% Kcal fat [22% MUFA. 9% SFA]; HISAT, 38% Kcal fat (11% MUFA, 20% SFA). The percentage of calories derived from protein and carbohydrates were 15% and 47% respectively, and cholesterol levels constant (300mg/day) for both diets. Each diet was consumed for 8 with a 2-month washout period. The preliminary data showed that the isoenergetic substitution with 11% Kcal MUFA for SFA significantly reduced plasma total cholesterol (-23.6±3.2mg/dl, p<0.0001), LDL-C (12.4±4mg/dl, p<0.0002) as well as HDL (-9.1±5.6mg/dl, P<0.0001). Changes in triglyceride levels were not significant. These results the beneficial effect of long-term consumption of diets high in MUFA (Funding provided by the Department of Defense)

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Long-term Effects of Diets High in Monounsaturated Fatty Acid on Plasma Lipid Levels in Healthy Men and Women: The Macadamia Nut Study, Phase II
K H (Jenny) Tung, Carol Waslien, et. al.

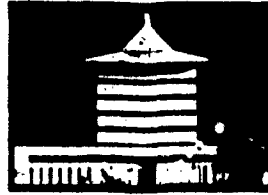**The Queen Emma Clinic Diabetes Classes**
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"CLINICAL TRIAL TO DETERMINE THE ABILITY OF A DIET HIGH IN MONOUNSATURATED FATTY ACIDS TO REDUCE RISK FACTORS FOR CORONARY HEART DISEASE"

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Effects of Diets High in Monounsaturated Fatty Acids on Plasma LDL subclasses in Healthy Men and Women: Macadamia Nut Study- Phase II. K.H. Tung, C. Washlen, P.J Elmer, J.D. Otvos, G. Wergowske, J.D. Curb. U. of Hawaii, Hawaii HI 96822, Kaiser Permanente, Portland, OR97227, North Carolina State U., Raleigh, NC 27965.

A randomized crossover feeding study with a macadamia nut based high monounsaturated fatty acids [MUFA] diet [HIMUFA] and a typical American diet [HISAT] high in Saturated fatty acids [SAT] was conducted. Fatty acid profiles of the two diets were HIMUFA (38% fat: 9% SAT, 22% MUFA) and HISAT (38% fat: 20% SAT, 11% MUFA). 27 healthy volunteers age 20 to 52 years were fed two diets each lasting 8 weeks with a 2-month wash-out in between. Fasting plasma lipids as well as LDL subclasses were measured on week 5 and the last two consecutive days of week 8 of each diet using NMR. Overall, the mean plasma total Cholesterol [TC] was significantly lower (11.6%, $p<0.0001$) in HIMUFA than in HISAT, as was the mean LDL (13.1%, $p<0.0002$). The reduction of LDL levels was exclusively in the largest particles (LDL_3; 28.5%, $p<0.0001$). Both LDL_2 (intermediate) and LDL_1 (small) tended to increase in HIMUFA but the changes were not significant. The mean particle concentration (12.1%, $p<0.0001$) as well as the mean size (0.70%, $p<0.01$) of LDL was significantly decreased in HIMUFA compared to HISAT. The cholesterol lowering effects in TC and LDL of HIMUFA is very promising, however, further investigations are needed to evaluate the LDL subclass effects of HIMUFA on CHD risk.

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Serum Lipid Effects of a High–Monounsaturated Fat Diet Based on Macadamia Nuts

J. David Curb, MD; Gilbert Wergowske, MD; Joan C. Dobbs, PhD; Robert D. Abbott, PhD; Boji Huang, MD, PhD

Background: Recent studies have identified potential beneficial effects of eating nuts, most of which have substantial amounts of monounsaturated fats. Macadamia nuts are 75% fat by weight, 80% of which is monounsaturated.

Objective: To examine variations in serum lipid levels in response to a high–monounsaturated fat diet based on macadamia nuts.

Methods: A randomized crossover trial of three 30-day diets was conducted in 30 volunteers aged 18 to 53 years from a free-living population. Each was fed a "typical American" diet high in saturated fat (37% energy from fat); an American Heart Association Step 1 diet (30% energy from fat); and a macadamia nut–based monounsaturated fat diet (37% energy from fat) in random order. Serum total cholesterol, high-density lipoprotein cholesterol, and triglyceride levels were measured.

Results: Mean total cholesterol level after the typical American diet was 5.20 mmol/L (201 mg/dL). After the Step 1 diet and the macadamia nut diet, total cholesterol level was 4.99 mmol/L (193 mg/dL) and 4.95 mmol/L (191 mg/dL), respectively. Low-density lipoprotein cholesterol level was 3.37 mmol/L (130 mg/dL) (typical diet), 3.21 mmol/L (124 mg/dL) (Step 1 diet), and 3.22 mmol/L (125 mg/dL) (macadamia nut diet). High-density lipoprotein cholesterol level was 1.43 mmol/L (55 mg/dL) (typical), 1.34 mmol/L (52 mg/dL) (Step 1), and 1.37 mmol/L (53 mg/dL) (macadamia nut). Lipid values after the Step 1 and macadamia nut diets were significantly different from those after the typical diet ($P<.05$).

Conclusions: The macadamia nut–based diet high in monounsaturated fat and the moderately low-fat diet both had potentially beneficial effects on cholesterol and low-density lipoprotein cholesterol levels when compared with a typical American diet.

Arch Intern Med. 2000;160:1154-1158

From the Division of Clinical Epidemiology, Department of Medicine (Drs Curb, Wergowske, Abbott, and Huang), and Division of Geriatric Medicine (Drs Curb and Wergowske), John A. Burns School of Medicine, University of Hawaii at Manoa, Honolulu; Exploring New Concepts, Honolulu (Dr Dobbs); and Division of Biostatistics and Epidemiology, University of Virginia School of Medicine, Charlottesville (Dr Abbott).

RADITIONALLY, the inhabitants of regions such as Greece and southern Italy, where rates of coronary heart disease are low, have consumed relatively high-fat diets containing substantial amounts of olive oil, a substance with high concentrations of the monounsaturated fatty acid oleic acid.[1,2] These "Mediterranean diets" frequently contain more energy from fat than the typical American diet but are higher in monounsaturated fats. Less than 10% of energy in such diets comes from saturated fats.

A number of studies have demonstrated apparently beneficial effects of diets based on high monounsaturated fatty acid content primarily derived from olive oil.[3-5] Few have looked at the effects of whole complex foods high in monounsaturated fatty acids. Nuts are a complex food that contains considerable amounts of mo-

nounsaturated fat, and they have also long been part of the traditional diet in many Mediterranean countries. Recent studies have shown potential beneficial effects of tree nuts in the diet.[6-8] The macadamia nut, a tree nut that originated in Australia, has become a primary export crop from Hawaii in recent years. The macadamia nut is approximately 75% fat by weight, with 88% of its energy from fat. Monounsaturated fatty acids are the predominant fat. Oleic acid is the predominant monounsaturate, but a considerable portion is palmitoleic acid, a component not present in substantial amounts in olive oil. Macadamia nuts are a complex food with large amounts of carbohydrates and fiber as well as a number of vitamins and minerals.[9]

Because of the high fat content of the macadamia nut, it has popularly been thought to be bad for health. However, since some nuts, including the macadamia nut, could be substituted for food

SUBJECTS AND METHODS

The study was a controlled, crossover design feeding study of three 30-day dietary options. Subjects eligible to participate were men and women with a fasting cholesterol level above 3.9 mmol/L (150 mg/dL) and a triglyceride level below 4.5 mmol/L (400 mg/dL); taking no current pharmacological treatment for hyperlipidemia; between 18 and 55 years of age; weighing between 80% and 130% of ideal weight; with no history of diabetes mellitus or pancreatic insufficiency, or an unstable medical condition of any kind; having no history of food allergies, especially to tree-grown nuts; and not pregnant, breastfeeding, or taking certain birth control pills. Approximately 450 individuals were screened by telephone or in person. Forty-two individuals participated in the run-in. Of these, 16 men and 18 women began the experimental diet period, of whom 15 men and 15 women completed the study.

To minimize study group imbalance resulting from dropouts or exclusions during the run-in or early in the first dietary period, dietary assignments were randomly made in 2 phases. Both randomizations were stratified by sex. For the first dietary period, subjects were randomized to 1 of the 3 study diets. Subsequently, during the later part of the first diet period, subjects were randomized to the remaining diets they would follow during the next 2 periods. Thus, randomization remained balanced throughout the study, and all subjects had equal probability of being in each of the 3 diet sequences, despite several early dropouts. Study personnel involved in performing measurements and analyses were blinded to the diet sequences. To avoid dropouts, telephone screening, individual and group meetings, and a 6-day run-in period were used to screen participants for compliance and willingness to accept the restrictions imposed by the dietary regimens.

Every day, the subjects ate breakfast and dinner at the study site and were given a bag lunch prepared by study personnel. The one exception was Saturday night, when participants were allowed a "free" meal with specific guidelines on the amount of fat consumed. Additional energy was made available in the form of "unit" foods consumed ad libitum in addition to the subjects' diet regimen, as long as they maintained their weight. These were in the form of 420-kJ (100-kcal) muffins or 420- and 840-kJ (100- and 200-kcal) packages of chili, developed to match the nutrient profile for each diet. Body weight was measured 2 times per week, and energy intake levels were altered when necessary to maintain each subject's weight. A daily diary was used to monitor illness, medication use, and deviations from usual physical activity patterns or the study diet.

The diets used were a "typical American" diet, a macadamia nut diet high in monounsaturated fat, and an AHA Step 1 "prudent" diet. A 10-day cycle menu was designed with the Genesis Ingredient Database (ESHA Research, Portland, Ore) with the use of whole foods to match the nutrient profile. All 3 diets were designed to contain 17% of total energy from protein, with the percentage of energy from carbohydrate and fat depending on the diet (46% for the AHA Step 1 and macadamia nut diets; 53% for the typical American diet). Polyunsaturated fatty acids (7%) and cholesterol content (300 mg) of all diets were kept constant. Up to 5 alcoholic beverages a week were allowed, as were 5 non–energy-containing beverages with caffeine per day. The foods were prepared by means of recipes and methods similar to those commonly used in which the experimental diets are adapted to contain modified amounts of the appropriate foods and nutrients. For the macadamia nut diet, finely ground macadamia nuts were used.

After a 12- to 14-hour fast, each subject had blood drawn on the last 3 consecutive days of each dietary period, with no alcoholic beverages allowed in the 5 days before a blood draw. Analyses for total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride levels were carried out at the Penn Medical Laboratory, Washington, DC, in 1 batch after the end of study with the use of serum specimens frozen at −70°C for 3 to 6 months. Cholesterol level was measured enzymatically using an autoanalyzer (Hitachi 717 Autoanalyzer; Hitachi Instruments Inc, San Jose, Calif),[11] and HDL cholesterol level was determined directly after manganese chloride–heparin precipitation. The laboratory was standardized according to the Lipid Standardization Program of the Centers for Disease Control and Prevention and the National Heart, Lung, and Blood Institute. Values for low-density lipoprotein cholesterol were calculated by subtraction by means of the Friedewald algorithm.[12] To reduce the impact of interindividual variability, the average of the 3 daily values at each time was used for statistical calculations. For each of the 3 dietary treatments, chemical analyses were conducted on homogenized samples of 4 complete days of the 10-day cycle menu (n = 12). Chemical analyses were conducted by Food Products Laboratory, Portland, Ore.

Body weight measurements were taken to the nearest 10th of a pound on a digital scale (Precision Health Scale UC-300; A & D Weighing, Milpitas, Calif) 2 times per week, before breakfast in street clothes, without shoes or heavy clothing.

This study was approved by the University of Hawaii institutional review board, Honolulu. All subjects gave written informed consent after thorough explanation of the study.

Statistical methods included linear models for the analysis of a 3-period crossover design.[13] Such models included variables for assessing the influence of diet, period, and carryover effects into subsequent dietary periods. Transforming the data by log transformations had no effect on the findings reported herein. All reported P values were based on 2-sided tests of significance.

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items high in saturated fat as a potential element in a healthy diet, we thought it would be valuable to investigate the effects of consuming a diet with a large percentage of energy derived from macadamia nuts. We report herein the results of a carefully controlled feeding study with a crossover design comparing a diet rich in macadamia nuts with 37% energy from fat; a "typical American" diet with 37% energy from fat; and a Step 1 diet conforming to the recommendations of the American Heart Association (AHA)[10] with 30% energy from fat.

Table 1. Mean Serum Concentrations of Lipids and Lipoproteins at the End of Each Dietary Period for All Subjects Combined and by Sex*

Lipid	Baseline Values		Typical American Diet		AHA Diet		Macadamia Nut Diet	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Total study group								
Cholesterol, mmol/L	5.31	0.86	5.20	0.79	4.99†	0.89	4.95†	0.84
(mg/dL)	(205.1)	(33.3)	(201.2)	(30.4)	(193.1)	(34.5)	(191.3)	(32.6)
LDL, mmol/L	3.47	0.77	3.37	0.66	3.21‡	0.79	3.22‡	0.76
(mg/dL)	(134.0)	(29.8)	(130.4)	(25.7)	(124.3)	(30.4)	(124.5)	(29.5)
Triglyceride, mmol/L	0.91	0.38	0.87	0.37	0.94‡	0.37	0.79‡	0.29
(mg/dL)	(80.2)	(33.1)	(77.5)	(32.7)	(83.6)	(32.6)	(70.4)	(26.0)
HDL, mmol/L	1.42	0.18	1.43	0.20	1.34§	0.19	1.37†	0.21
(mg/dL)	(55.0)	(6.8)	(55.3)	(7.6)	(52.0)	(7.2)	(52.8)	(8.2)
Men								
Cholesterol, mmol/L	5.30	0.88	5.26	0.71	5.01‡	0.86	5.04	0.73
(mg/dL)	(204.5)	(34.1)	(203.5)	(27.6)	(193.7)	(33.2)	(195.0)	(28.3)
LDL, mmol/L	3.50	0.74	3.47	0.58	3.28‡	0.71	3.40	0.64
(mg/dL)	(135.2)	(28.4)	(134.2)	(22.4)	(126.8)	(27.3)	(131.5)	(24.7)
Triglyceride, mmol/L	0.89	0.35	0.97	0.41	1.01	0.42	0.79‡	0.33
(mg/dL)	(78.3)	(30.8)	(82.0)	(36.3)	(89.8)	(36.8)	(70.0)	(28.9)
HDL, mmol/L	1.39	0.18	1.37	0.24	1.26§	0.21	1.28†	0.23
(mg/dL)	(53.6)	(6.8)	(52.8)	(9.1)	(48.9)	(8.0)	(49.5)	(9.0)
Women								
Cholesterol, mmol/L	5.33	0.87	5.15	0.71	4.98	0.95	4.85‡	0.96
(mg/dL)	(205.7)	(33.8)	(199.0)	(33.7)	(192.5)	(36.9)	(187.7)	(37.1)
LDL, mmol/L	3.44	0.83	3.27	0.75	3.15	0.88	3.04‡	0.85
(mg/dL)	(132.8)	(32.0)	(126.6)	(28.9)	(121.9)	(34.0)	(117.6)	(33.0)
Triglyceride, mmol/L	0.89	0.35	0.82	0.33	0.87	0.31	0.80	0.27
(mg/dL)	(78.3)	(30.8)	(73.0)	(29.1)	(77.5)	(27.6)	(70.8)	(23.9)
HDL, mmol/L	1.39	0.18	1.49	0.13	1.42‡	0.12	1.45	0.16
(mg/dL)	(53.6)	(6.8)	(57.8)	(4.9)	(55.0)	(4.8)	(56.0)	(6.0)

*AHA indicates American Heart Association; LDL, low-density lipoprotein; and HDL, high-density lipoprotein.
†$P<.01$ vs typical American diet.
‡$P<.05$ vs typical American diet.
§$P<.001$ vs typical American diet.

RESULTS

Sixteen (53%) of the 30 participants who completed the study were white, 11 (37%) were Asian-Pacific Islanders, and 3 (10%) were black. Ages ranged between 18 and 53 years, with a mean age of 36.7 years for men and 33.8 years for women. The mean body mass index (weight in kilograms divided by the square of the height in meters) of the men was 24 ± 2.4 (range, 19.5-27.9). The mean body mass index for the women was 22 ± 2.6 (range, 19.1-28.3). Only 1 subject had more than a 1.35-kg weight change during the study period (1.53-kg loss). No differences in skinfold thickness were seen throughout the study. The mean baseline cholesterol level ranged from normal to high. However, the majority of participants did not meet clinical criteria for hypercholesterolemia. In men, the mean baseline cholesterol level was 5.30 mmol/L (204.5 mg/dL) and ranged from 3.9 to 6.9 mmol/L (158 to 267 mg/dL). In women, the mean was 5.33 mmol/L (206 mg/dL) and ranged from 4.1 to 7.0 mmol/L (157 to 272 mg/dL) (**Table 1**). Triglyceride levels tended to be relatively low and HDL cholesterol levels relatively high compared with average American values. Energy requirements for subjects ranged from 6300 to 14 700 kJ (1500 to 3500 kcal) for women and 10 500 to 16 700 kJ (2500 to 4000 kcal) for men, somewhat higher than the range reported in many studies. A comparison between the ac-

tual macronutrient profiles expressed as percentage of energy consumed and those formulated with Genesis software is shown in **Table 2**. The differences between the values were minimal.

Shown in Table 1 are the mean and SD for lipid and lipoprotein factors at the baseline evaluation and at the end of each dietary period for the overall group and for the 2 sexes. Since the baseline free-living diets were not necessarily comparable, all statistical comparisons were made between values at the end of the dietary periods and not between changes from the baseline to the end of the diet period. Compared with the typical American diet, the mean total cholesterol level was significantly lower ($P<.01$) for the macadamia nut and AHA Step 1 diets. The mean low-density lipoprotein cholesterol level was also lower for these 2 experimental diets ($P<.05$). Mean triglyceride values were significantly higher than with the typical American diet ($P<.05$) for the Step 1 diet and significantly lower ($P<.05$) for the macadamia nut diet. The mean HDL cholesterol level was lower after the Step 1 ($P<.001$) and the macadamia nut ($P<.01$) diets. When men and women were compared, lipid profile trends were not statistically different.

When the mean cholesterol trends for each of the 6 randomization sequences were examined, there was a tendency for total cholesterol level to drop during the study period, in all randomization groupings, a phenomenon

Table 2. Energy Content and Nutritional Profile of Macronutrients as Planned and as Observed From Chemical Analyses of 12 Complete-Day Samples*

	% of Energy Intake					
	Typical American Diet		AHA Diet		Macadamia Nut Diet	
Nutrient	Planned	Observed	Planned	Observed	Planned	Observed
Protein	17	17	17	16	17	17
Carbohydrate	46	48	53	54	46	48
Total fat	37	35	30	30	37	35
Saturated	16	14	9	9	9	9
Polyunsaturated	7	9	7	7	7	6
Monounsaturated	14	12	14	15	21	20
Energy, kJ	13 422	13 797	13 778	14 322	13 724	14 288
Cholesterol, mg	300	305	300	297	300	300

*Diets were formulated and nutrients calculated by Genesis Software Version 4.2 from ESHA Research, Portland, Ore. AHA indicates American Heart Association.

that is common in individuals who become involved in studies in which their diets are controlled to a greater extent than in a free-living environment.[14] These trends did not exceed expectations, and there were no significant carryover effects between dietary periods. Adjustment for period effects demonstrated only minimal effects.

COMMENT

The 3 diets used in this investigation were designed both to evaluate substitution of monounsaturated fat (primarily derived from macadamia nuts) for saturated fat and to compare the high–monounsaturated fat diet with the lower-fat AHA Step 1 diet. The findings indicate that the macadamia nut–based high-fat (37%) diet and the moderately low-fat (30%) AHA Step 1 diet had similar effects on lipid profiles. The results suggest that replacing saturated fats in the typical American diet with monounsaturated fats present in macadamia nuts has a favorable effect on serum cholesterol concentrations of healthy adults. This effect was seen despite the fact that the study included a wide range of ethnic groups, had a broad age range, and included only relatively lean, healthy individuals of both sexes, many of whom had relatively low cholesterol concentrations. It should be noted that simply adding foods high in monounsaturated fats to the diet instead of substituting for foods high in saturated fats could be deleterious because of the adverse effects associated with weight gain. It is of interest that the results of the study were similar in men and women. Although women appeared to have somewhat greater lowering of cholesterol and low-density lipoprotein cholesterol levels with the experimental diets, the small sex-specific sample sizes may have contributed to these findings, and caution must be used in interpretation of the sex-specific results. Most previous studies either have been done only in men or have not reported sex-specific findings. These data would be most appropriately viewed as generating hypotheses for use in future investigations. A 30-day diet period is the minimum that should be used to see dietary effects on lipids. It is possible that the differences seen herein would be increased with a longer period for each diet.

Making direct comparisons between studies is difficult because of widely variable differences in the length of studies, the characteristics of the participants, and the range of fat, cholesterol, and fiber contents of diets used in the various studies. However, the results of this study are generally consistent with those seen in other studies contrasting high–monounsaturated fat diets to high–saturated fat and low-fat diets.[15-23] The magnitude of the decrease of serum cholesterol level with both the moderately low-fat and the high–monounsaturated fat diets in this study is lower than in some studies. On the other hand, the decrease in triglyceride levels with the macadamia nut diet is larger than that reported in most other similar studies. The 4.5% lower HDL cholesterol level with the macadamia nut diet compared with the high-fat diet is greater than the changes seen in some other published studies, which generally report anywhere from a 2% increase to a 6% drop.[15-23] The differences in lipid levels, including those in HDL cholesterol level, are similar to those seen in the recently reported Dietary Effects on Lipoproteins and Thrombogenic Activity (DELTA) study, which also compared diets that replaced saturated fats with monounsaturated fats or carbohydrates and that had a nutrient profile similar to that used in this study.[23] Such changes in HDL cholesterol level are significant and potentially important. However, Hegsted et al[4] pointed out that the effects of diet on HDL cholesterol level are complex and may not be subject to meaningful interpretation. Thus, interpretation of the HDL results of the present study may also be difficult. In general, the changes in HDL cholesterol level induced by diet are relatively small, the day-to-day variation is large, and the clinical significance of such changes is not known.[24] Further investigation of HDL effects is longer-term studies with close attention to other dietary components is warranted.

Given the data available on the effects of monounsaturated fats in the diet and the nutrient composition of the macadamia nut, a beneficial effect could be hypothesized. However, nuts are complex foods that contain many nutrients, and macadamia nuts have a fatty acid profile that differs somewhat from that of most common sources of monounsaturated fatty acids in the diet. One of these monounsaturated fatty acids, palmitoleic acid, was reported to increase cholesterol level in one study.[25] The current study was not designed to examine the effects of individual fatty acids, but the overall ef-

fect of the macadamia nut–based diet was within the range of that seen in other short-term feeding studies. In addition, the magnitude of the cholesterol-lowering effect of a diet high in monounsaturated fatty acids is similar to that of a Step 1 diet as seen in other such studies.

An epidemiological study of California Adventists was one of the first to suggest the potential health benefits of nuts.[26] That study suggested that regular consumption of nuts had a protective effect against coronary heart disease in that population. Dietary studies of the walnut and the almond have provided more specific evidence of the potential cholesterol-lowering properties of this group of foods.[6-8] As with all high-fat foods, nuts may be an important source of energy, and, if not substituted for other fatty foods, they could result in weight gain.

However, in a pilot study for the present study in which 70 healthy free-living subjects were randomized to groups given supplements of 90 g (2688 kJ) or 45 g (1344 kJ) of macadamia nuts as a supplement, or to a regular diet group, there was no significant change in the mean weight of any of the groups after 1 month.[27] All groups received only a single 15-minute dietary counseling session on food substitutions to avoid weight gain and eating a healthy diet. Some participants in that study reported a suppression of appetite after eating their nuts each day. Eating nuts may be associated with increased satiety, but few data are available.

No important side effects of consistent ingestion of large amounts of macadamia nuts were noted in either the pilot study or the feeding study. In the pilot study, gastrointestinal tract discomforts consistent with those experienced with radical shifts in dietary fat content were not uncommon but usually temporary. There was no difference in serum cholesterol level between the groups in the pilot study, although the high-dose macadamia nut group ate 50% of their energy as fat.

CONCLUSIONS

In conclusion, the results of this study indicate that the consumption of a diet high in monounsaturated fats, a significant proportion of which were derived from macadamia nuts, appears to lower serum cholesterol level when total energy balance and percentage of energy from fat are maintained. In addition, the effect of such a diet on levels of cholesterol and other lipids was not statistically different from that seen with a lower-fat AHA Step 1 diet, except for lowering of triglyceride levels by the macadamia nut–based diet. These results, coupled with the palatability of macadamia nuts, suggest that physicians can recommend the consumption of these and other nuts as part of a satisfying and healthy diet.

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